

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
10 August 2006 (10.08.2006)

PCT

(10) International Publication Number  
WO 2006/083986 A2(51) International Patent Classification:  
C12Q 1/68 (2006.01)(21) International Application Number:  
PCT/US2006/003611

(22) International Filing Date: 1 February 2006 (01.02.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/649,208 1 February 2005 (01.02.2005) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: BIOMARKERS FOR TISSUE STATUS

(57) Abstract: The invention relates to methods of accurately and quickly diagnosing and monitoring the progression of cancer and ischemically injured tissue. The invention also provides methods of treatment as well as methods of screening for compositions useful for treating the disorders.

WO 2006/083986 A2

## BIOMARKERS FOR TISSUE STATUS

### RELATED APPLICATIONS

This application claims priority to US Provisional Patent Application Ser. No. 60/649,208, filed February 1, 2005, entitled "Biomarkers for Tissue Status" and is hereby incorporated by reference in its entirety.

### GOVERNMENT SUPPORT

This work described herein was supported by the National Institutes of Health.

### BACKGROUND OF THE INVENTION

Tumors have been likened to wounds that do not heal, suggesting that tumorigenic processes may share common, or at least analogous, regulatory mechanisms to wound healing.

Introduction

The processes of tissue regeneration and tumorigenesis are both complex, adaptive processes controlled by cues from the tissue microenvironment. There are various signals that orchestrate a response to injury that results in regeneration and tissue repair of a wound. Tissue regeneration and carcinogenesis both involve processes, such as cell proliferation, survival, and migration, that are controlled by growth factors, cytokines as well as inflammatory and angiogenic signals. Signals facilitating cell proliferation, survival, and invasiveness derive from multiple cellular and extracellular sources in the microenvironment of wounds and cancer. Therefore, wounds and cancer share a number of phenotypes in cellular behavior, signaling molecules, and gene expression. Understanding the similarities between wounds and cancers can reveal new insights into the malignant properties of cancers.

The identification of tumor markers suitable for the early detection and diagnosis of cancer holds great promise to improve the clinical outcome of patients. It is especially important for patients presenting with vague or no symptoms or with tumors that are relatively inaccessible to physical examination. Despite considerable effort directed at early detection, no cost effective screening tests have been developed.

Kidney is a member of a restricted class of organs capable of regeneration and repair following traumatic events such as ischemia/reperfusion injury, which is the major cause of

acute renal failure (ARF) in both native (Rabb H and Martin JG 1997) and transplanted kidney (Shoskes DA, and Halloran PF (1996)). In the majority of cases of non-chronic ARF, kidney tissue regenerates and regains complete functionality in the absence of persistent inflammation and fibrosis, even when the initial injury and functional decline are very pronounced (Ysebaert DK et al 2004). The process of renal regeneration and repair (RRR) begins shortly after injury, a period during which necrotic cells are accompanied by replicating cells lining the injured proximal renal tubule. The commitment to DNA synthesis in this population of proliferating cells occurs rapidly, temporally coinciding with the emergence of morphologic and functional derangements. Ischemia/reperfusion injury, regeneration and recovery are part of the same continuum of biological responses and depend on the coordination of the cell-cycle machinery as well as the cells' ability to survive the initial injury (Price PM et al 2004). Clinically and biologically, ischemic ARF is a complex but orderly continuum that can be separated into a series of four overlapping phases that have been referred to as "initiation," "extension," "maintenance," and "recovery" (Sutton TA et al 2002).

Renal cell carcinoma (RCC) accounts for 3% of all adult male malignancies in the United State (Jemal A. et al 2004) and is a clinicopathologically heterogeneous disease that includes several histologically distinct cellular subtypes. A majority of the published evidence suggests that proximal renal tubules are the sites from which malignant RCC cells originate, although a recent study offers evidence that such cells may also originate from distal tubules (Motzer RJ et al 1996; Mandriota SJ et al 2002). A number of genetic syndromes predispose to the development of RCC, and genes associated with five of these syndromes are identified: von Hippel-Lindau (VHL), met proto-oncogene (MET), fumarate hydratase (FH), Birt-Hogg-Dube syndrome (BHD) and hyperparathyroidism 2 (HRPT2) (Pavlovich and Schmidt 2004). RCC also frequently develops in conjunction with polycystic kidney disease and renal allografts, both of which conditions induce a chronic regenerative response (Brennan et al 1991, Gomez Garcia I et al 2004).

There is a need in the art to understand the similarities between wounds and cancers and for the identification of tumor markers suitable for the detection and diagnosis of the molecular changes in cancers, acute organ failure, wound healing and organ transplantation. There is also a need in the art to develop new therapeutic biomarkers and compositions. Thus, it is desirable to have a reliable and accurate method of determining the renal status in patients, the results of which can then be used to manage their treatment.

## BRIEF SUMMARY OF THE INVENTION

The present invention provides sensitive diagnostic and therapeutic methods using markers for RCC, acute renal failure, RRR, organ transplantation, organ shipment, wound healing, tumors, and organ failure. Also provided are methods for screening for compounds to be used in the therapeutic methods.

The measurement of these markers in patient samples provides information that diagnosticians can correlate with a probable diagnosis of human cancer, ischemia, organ failure, wound healing, tissue regeneration, tissue repair, or a negative diagnosis (*e.g.*, normal or disease-free).

Provided herein are methods of qualifying the tissue status in a subject comprising measuring at least one biomarker in a sample from the subject, wherein the biomarker is selected from the group consisting of the markers listed in one or more of Tables 7, 8, 9, 13, 20, and 23 and correlating the measurement with tissue status.

In one embodiment, the methods further comprise managing treatment of the subject based on the status, wherein managing treatment is selected from ordering more tests, performing surgery, chemotherapy, dialysis, treatment of acute organ failure, organ transplantation, wound healing treatment, and taking no further action.

In a related embodiment, the methods may further comprise measuring the at least one biomarker after subject management.

In one embodiment, the tissue status is selected from the group consisting of the subject's risk of cancer, regeneration, tissue repair, acute organ failure, organ transplantation, the presence or absence of disease, the stage of disease and the effectiveness of treatment of disease.

In a related embodiment, the methods may further comprise measuring at least two biomarkers in a sample from the subject and correlating measurement of the biomarkers with renal status.

In one embodiment, the biomarkers are selected from one or more of Tables 7, 8, 9, 13, 20, and 23. In a related embodiment, the biomarkers are selected from any one or more of Cluster 1 – 27. In another related embodiment, the biomarkers are selected from any one or more of discordant genes. In another related embodiment, the biomarkers are selected from any one or more of concordant genes.



The invention provides, in one embodiment, measuring comprising providing a nucleic acid sample from the subject; and capturing one or more of the biomarkers on a surface of a substrate comprising capture reagents that bind the biomarkers. In a related embodiment, the substrate is a nucleic acid chip. In another related embodiment, the nucleic acid chip is an RNA or DNA or oligo-nucleotide chip. In a related embodiment, the substrate is a microtiter plate comprising biospecific affinity reagents that bind the at least one biomarkers and wherein the biomarkers are detected by fluorescent labels.

In one embodiment, the measuring is selected from detecting the presence or absence of the biomarkers(s), quantifying the amount of marker(s), and qualifying the type of biomarker.

The invention provide, in one embodiment, measuring at least one biomarker using a biochip array. In one embodiment, the biochip array is an antibody chip array, tissue chip array, protein chip array, or a peptide chip array. In a related embodiment, the biochip array is a nucleic acid array. In another related embodiment, at least one biomarker capture reagent is immobilized on the biochip array. In yet another related embodiment, the protein biomarkers are measured by immunoassay.

In one embodiment, correlating is performed by a software classification algorithm.

The invention provides, in one embodiment, samples selected from one or more of blood, serum, kidney, renal tumor, renal cyst, renal metastasis, plasma, urine, saliva, and feces. In a related embodiment, the tissue is normal or malignant or ischemic, healing kidney, liver, lung, heart, esophagus, bone, intestine, breast, prostate, brain, uterine cervix, testis, stomach or skin.

In one aspect, the invention provides methods of diagnosing renal status in a subject, comprising determining the pattern of expression of one or more markers listed in one or more of Tables 7, 8, 9, 13, 20, and 23 in a sample from the subject, wherein a differential expression pattern of the one or more markers in a subject is indicative of cancer, acute renal failure, ischemia, or organ transplantation.

In one embodiment, the determining is of any one or more of Trends 1 – 27. In a related embodiment, the determining is of any one or more of clusters 1 – 27.

In another aspect, the invention provides methods comprising measuring a plurality of biomarkers in a sample from the subject, wherein the biomarkers are selected from one or more of the group consisting of one or more of Tables 7, 8, 9, 13, 20, and 23 or Clusters 1 – 27.

According to another aspect, the invention provides kit comprising a capture reagent that binds a biomarker selected from Table 9 or Cluster 1 – 27 and combinations thereof; and a container comprising at least one of the biomarkers.

In one embodiment, the capture reagent binds a plurality of the biomarkers. In a related embodiment, the capture reagent is a nucleic acid probe. In yet another related embodiment, the kit further comprises a second capture reagent that binds one of the biomarkers that the first capture reagent does not bind.

According to another aspect, a kit is provided comprising a plurality of capture reagents that binds one or more biomarkers selected from Table 9 or Cluster 1 – 27. In one embodiment, the at least one capture reagent is an antibody or a nucleic acid complementary to the biomarker. In a related embodiment, the kit further comprises a wash solution that selectively allows retention of the bound biomarker to the capture reagent as compared with other biomarkers after washing. In another related embodiment, the kit further comprises instructions for using the capture reagent to detect the biomarker. In one embodiment, the kit detects of one or more of renal cancer, renal regeneration, renal repair, acute renal failure, ischemia or kidney transplantation. In a related embodiment, the instructions provide for contacting a test sample with the capture agent and detecting one or more biomarkers retained by the capture agent.

In one aspect, the invention provides methods of monitoring the treatment of a subject for renal carcinoma, comprising determining one or more pre-treatment expression profiles of markers described in Table 9, in a cell of a subject administering a therapeutically effective amount of a candidate compound to the subject, and determining one or more post-treatment expression profiles of markers described in Table 9, in a cell of a subject, wherein a modulation of the expression profile indicates efficacy of treatment with the candidate compound.

In one embodiment, a pre-treatment expression profile of at least one discordantly or concordantly expressed gene indicates renal carcinoma. In a related embodiment, a post-treatment expression profile of at least one discordantly or concordantly expressed gene indicates the efficacy of the treatment. In another related embodiment, the expression profile is determined by a nucleic acid array method.

In one aspect, the invention provides methods of identification of a candidate molecule to treat renal carcinoma, comprising contacting a cell with a candidate molecule and detecting the expression profile of a target the cell, wherein if the expression profile is of one or more of

at least one discordantly and/ or concordantly expressed gene the molecule may be useful to treat renal carcinoma, acute renal failure, ischemia, kidney transplantation, organ shipment, cancer or wound healing of regenerative tissues

In one embodiment, the candidate molecule is one or more of a small molecule, a peptide, or a nucleic acid. In a related embodiment, the small molecule is one or more of the molecules listed in Table 9 or Clusters 1 – 27.

In another embodiment, the method further comprises comparing the expression profile to a standard expression profile. In a related embodiment, the standard expression profile is the corresponding expression profile in a reference cell or population of reference cells. In another related embodiment, the reference cell is one or more cells from the subject, cultured cells, cultured cells from the subject, or cells from the subject pre-treatment.

The invention provides, in one aspect, methods of identifying a diagnostic marker comprising obtaining a sample from an ischemically injured kidney, obtaining a sample from a normal kidney, identifying genes having differential expression in the ischemically injured kidney compared to the normal kidney; and selecting at least one gene as a diagnostic marker for the cancer, acute organ failure, ischemia or organ transplantation.

In one embodiment, the method further comprises obtaining a sample from a cancerous kidney, identifying genes having a differential expression in normal kidney as compared to the cancerous kidney, comparing the genes having a differential expression, identifying genes having an differential expression in the ischemically injured kidney but not in the cancerous kidney; and selecting at least one gene as a diagnostic marker of a cancer of the first cell type.

One aspect provides methods of identifying a gene expression signature in a sample comprising determining the gene expression profile of a sample and comparing the expression profile to Trends 1 – 27.

In one embodiment, a similar signature to one or more of Trends 1 – 27 indicates the renal status. In a related embodiment, an inverted signature to one or more of Trends 1 – 27 indicates similar pathologies, drugs, toxins and conditions inducing cancer, ischemia, regeneration, repair, wound healing, acute organ failure. In another related embodiment, the gene expression signature is used it identify promoters and transcription factors that regulate the differential gene expression signatures listed in Table 9 and Trends 1 – 27. In yet another related embodiment, a signature that does not correspond to one or more of Trends 1 – 27 indicates a new trend.

The invention provides, in one aspect, the use of compounds identified according to the methods of certain embodiments and aspects in the treatment of cancer or as anti-cancer drugs, acute renal failure drugs, ischemia drugs, and kidney transplantation drugs.

In one aspect, the invention provides, a bioinformatics tool and method comprising code that accesses data attributed to a sample, the data comprising measurement of at least one biomarker in the sample, the biomarker selected from the group consisting of the markers listed in Table 9 and code that executes a classification algorithm that classifies the renal status of the sample as a function of the measurement.

In one embodiment, the classification algorithm classifies the renal status of the sample as a function of the measurement of a biomarker selected from the group consisting of: the markers listed in Table 9, the markers Cluster 1 – 27, or Trends 1 – 27.

In one embodiment, the classification algorithm classifies the renal status of the sample as a function of the measurement of one or more of the biomarkers listed in Table 9, Cluster 1 – 27, or Trends 1 – 27.

In one embodiment, the classification algorithm classifies the renal status of the sample as a function of the measurement of one or more of the biomarkers listed in Table 9, Cluster 1 – 27, or Trends 1 – 27.

According to one aspect, methods comprising communicating to a subject a diagnosis relating to renal cancer status determined from the correlation of biomarkers in a sample from the subject, wherein said biomarkers are selected from the group consisting of the biomarkers listed in Table 9 or Clusters 1 – 27 are presented.

In one embodiment, the diagnosis is communicated to the subject via a computer-generated medium.

In one aspect, the invention provides, a method for identifying a candidate compound to treat renal carcinoma, comprising contacting renal carcinoma cancer cell with a test compound and determining the expression profile of one or more of the markers listed in Table 9 in the cancer cell, ischemic cell or the healing cell.

In one embodiment, the candidate compound is generated by the software program and database as PharmaProjects. In another embodiment, the software is any software correlating genes to drug candidates. In a related embodiment, the invention provides methods for screening for combination therapies, e.g., one or more the compounds linked or generated by the software program and database as PharmaProjects (PJP Publications, LTD, England).

In another aspect, the invention provides, methods for modulating the renal profile a cell or group of cells comprising contacting a cell with one or more compounds linked or generated by the software program and database as PharmaProjects or a compound identified in the methods described herein.

5 In one embodiment, the methods further comprise determining the renal status of the cell or group of cells before the contacting.

In another embodiment, the methods further comprise determining the renal status of the cell or group of cells after the contacting.

10 In one embodiment, the determining the renal status of the cell is by determining one or more of the expression profiles of the markers listed in Table 9, Cluster 1 – 27, or Trends 1 – 27.

According to another aspect, method of treating a condition in a subject comprising administering to a subject a therapeutically effective amount of a compound which modulates a renal profile, wherein a modulation from a renal cell carcinoma profile to a tissue  
15 regeneration, tissue repair profile, or a normal profile indicates the efficacy of the treatment is presented.

In one embodiment, the renal profile is measured by gene expression profiling.

In certain embodiments, the methods further comprise managing subject treatment based on the status determined by the method. For example, if the result of the methods of the  
20 present invention is inconclusive or there is reason that confirmation of status is necessary, the physician may order more tests. Alternatively, if the status indicates that surgery is appropriate, the physician may schedule the patient for surgery. Likewise, if the result of the test is positive, e.g., the status is late stage renal cancer or if the status is otherwise acute, no further action may be warranted. Furthermore, if the results show that treatment has been  
25 successful, no further management may be necessary.

Preferred methods of measuring the biomarkers include use of a biochip array. Biochip arrays useful in the invention include protein and nucleic acid arrays. One or more markers are captured on the biochip array and subjected to laser ionization to detect the molecular weight of the markers. Analysis of the markers is, for example, by molecular  
30 weight of the one or more markers against a threshold intensity that is normalized against total ion current. Preferably, logarithmic transformation is used for reducing peak intensity ranges to limit the number of markers detected.

In preferred methods of the present invention, the step of correlating the measurement of the biomarkers with renal status is performed by a software classification algorithm. Preferably, data is generated on immobilized subject samples on a biochip array, by subjecting said biochip array to analysis; and, transforming the data into computer readable form; and  
5     executing an algorithm that classifies the data according to user input parameters, for detecting signals that represent markers present in subject and are lacking in non-cancer subject controls.

The markers are characterized by their transcript expression and/or by their known protein identities. The markers can be resolved in a sample by using a variety of techniques,  
10     e.g., nucleic acid chips, PCR, real time PCR, reverse transcriptase PCR, real time reverse transcriptase PCR, in situ PCR, chromatographic separation coupled with mass spectrometry, protein capture using immobilized antibodies or by traditional immunoassays.

The invention relates to methods for diagnosing and prognosing cancer, acute renal failure, ischemia, kidney transplantation, tissue regeneration and/or tissue repair by utilizing  
15     general as well as tissue-specific genetic markers, methods for identifying these markers, and the markers identified by such methods.

In one aspect, the invention provides methods of diagnosing renal status in a subject comprising determining the pattern of expression of one or more markers listed in Table 9 in a sample from the subject, wherein a differential expression pattern of the one or more markers  
20     in a subject free of cancer is indicative of cancer.

In one embodiment, the invention contemplates any of the polynucleotides in Table 6 and polynucleotides that are at least 70% identical to the sequences of the polynucleotides encoding the tumor markers listed in Table 9.

In one aspect, the concordant and discordant gene expression signatures can be used to  
25     search global gene expression data bases (e.g., GEO profiles) and datasets for similar signature or inverted signature and as such to identify tumors and pathologies that share the same signature, new drug that will invert the signature, or toxins that can cause cancer or wounds.

In one aspect, provided herein are methods for identifying a candidate compound to treat renal carcinoma, comprising contacting renal carcinoma cancer cell with a test  
30     compound; and determining the expression profile of one or more of the markers listed in one or more of Tables 7, 8, 9, 13, 20, or 23 in the cancer cell. In one embodiment, the candidate compound is identified by software program as the software program and database PharmaProjects.

In one aspect, provided herein are methods for modulating the renal profile a cell or group of cells comprising contacting a cell with one or more compounds identified by the software program and data base as PharmaProjects or a compound identified in the method described herein.

5 In one embodiment, methods may further comprise determining the renal status of the cell or group of cells before the contacting.

In one embodiment, methods may further comprise determining the renal status of the cell or group of cells after the contacting.

10 In one embodiment, the determining the renal status of the cell is by determining one or more of the expression profiles of the markers listed in one or more of Tables 7, 8, 9, 13, 20, or 23, Cluster 1 – 27, or Trends 1 – 27.

In one aspect, provided herein are methods treating a condition in a subject comprising administering to a subject a therapeutically effective amount of a compound which modulates a renal profile, wherein a modulation from a renal cell carcinoma profile to a tissue  
15 regeneration, tissue repair profile, or a normal profile indicates the efficacy of the treatment.

In one embodiment, renal profile is measured by gene expression profiling.

In one embodiment, methods may further comprise co-administering a therapeutically effective amount of a second compound which modulates a renal profile.

20 In one embodiment, the compound is a compound listed in one or more of Tables 7, 8, 9, 13, 20, or 23.

In one aspect, biomarkers for renal status are provided and comprise one or more of the transcripts listed in one or more of Tables 7, 8, 9, 13, 20, or 23.

In one embodiment, the biomarker differentiates tissue regeneration, tissue repair and cancerous tissue from normal tissue.

25 In one aspect, provided herein are methods method of qualifying the renal status in a subject comprising (a) measuring at least two biomarkers in a sample from the subject, wherein the biomarkers are selected from the group consisting of the markers listed one or more of Tables 7, 8, 9, 13, 20, or 23; and (b) correlating the measurement with renal status.

30 In one embodiment, methods may further comprise (c) managing treatment of the subject based on the status.

In one embodiment, methods may further comprise (d) measuring the at least one biomarker after subject management.

In one embodiment, the renal status is selected from the group consisting of the subject's risk of cancer, regeneration, tissue repair, acute organ failure, organ transplantation, the presence or absence of disease, the stage of disease and the effectiveness of treatment of disease.

5 In one embodiment, the biomarkers are selected from any one or more of Cluster 1 – 27.

In one embodiment, the biomarkers are selected from any one or more of discordant genes.

10 In one embodiment, the biomarkers are selected from any one or more of concordant genes.

In one embodiment, providing a nucleic acid sample from the subject; and capturing one or more of the biomarkers on a surface of a substrate comprising capture reagents that bind the biomarkers.

In one embodiment, wherein the substrate is a nucleic acid chip.

15 In one embodiment, the sample is selected from one or more of blood, serum, kidney, renal tumor, renal cyst, renal metastasis, kidney cell or cells, kidney tissue, plasma, urine, saliva, and feces.

In one embodiment, the tissue is kidney tissue.

Other embodiments of the invention are disclosed *infra*.

#### 20 BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 depicts is A) as schematic flow of the five-step comparison of global gene expression in RRR and RCC. B. Renal ischemia reperfusion protocol: 5-week-old C57BL/6 female mice were subjected to 50 minutes of left unilateral warm ischemia, followed by reperfusion.

25 Before the ischemia (normal kidney) or after the desired period of reperfusion (0, 6 or 12 h or 1, 2, 5, 7 and 14 days) both kidneys were rapidly excised. Histological studies were carried out for both kidneys. Microarray analysis was carried out using total RNA from the left kidney sampled before or immediately after ischemia or on days 1, 2, 5 and 14 of RRR. C. Venn diagram: 984 genes on the array were previously reported to be differentially expressed in RCC and normal kidney. Comparison with the current microarray study identified 1,325 genes differentially expressed in RCC and normal kidney. 361 genes were differentially expressed in both RRR and RCC. D. Venn diagram of the 361 genes differentially expressed



in both RRR and RCC, 278 gene were concordantly expressed, and 83 genes were discordantly expressed. E. Distribution of the 361 genes differentially expressed in both RRR and RCC.

5           Figure 2 depicts the results of a histological analysis. The renal ischemia reperfusion started with a damage followed by regeneration and healing.

Figure 2A-C depict renal tubular injury over the time interval studied. A) Essentially normal murine renal cortex taken at time 0 (H&E, 400x). B) Acute tubular necrosis two days after the ischemic event. About half of the tubules show complete necrosis with loss of epithelium and the remaining tubules show cells with reactive nuclear changes (hyperchromasia, prominent nucleoli) (H&E, 600x). C) Representative renal cortex 14 days after the ischemic event. Most of the tubules show a normal appearance with rare tubules showing degenerative or regenerative changes (H&E, 600x).

Figures 2D – G depict Proliferation of renal tubular epithelial cells in response to acute ischemic injury. Sections of mouse kidney were stained with antibody to MiB-1. D) Normal renal cortex at time 0. Only rare tubular cells are positive for MiB-1. E) Renal cortex taken 12 hours after ischemic event. The number of positive cells is similar to that of normal cortex. F) Renal cortex taken at 2 days after the ischemic event. Many tubular epithelial cells now stain positively for MiB-1. G) Renal cortex taken 7 days after ischemic event. Although scattered tubules still show multiple nuclei positive for MiB-1, most tubules are now negative or show rare individual cells with positive staining. (A-D, anti-MiB-1, 600x). Figures 2 H – K depict the immunoreactivity for Glut-1. Sections of mouse kidney taken at different time points were stained with antibody to Glut-1. H) Normal renal cortex taken at time 0. Positive staining is seen mainly in the distal collecting tubules. I) Renal cortex taken at 12 hours after ischemic event. In addition to distal collecting tubules, some proximal tubules are also staining. J) Renal cortex taken at 24 hours after ischemic event. More than half of cortical tubules now show some degree of staining for Glut-1. K) Renal cortex taken at 48 hours after ischemic event. Most tubules are now negative and the staining pattern is similar to that seen at time 0. (A-D, anti Glut-1, 400x).

30           Figure 3 depicts the RRR gene expression signature defined three large subsets of early, late and continuously changed genes. A total of 39 kidneys (normal, ischemic, immediately following ischemia and RRR for 1, 2, 5 and 14 days) were each analyzed separately on a microarray. The samples clustered into a dendrogram of two parent branches: the first normal and ischemic kidneys and second parent branch of genes continually changed

at days 1, 2, 5 and 14 days (\*). The second branch clustered further into an early branch (A) that included days 1 and 2 and the late branch (B) that included days 5 and 14 following ischemic renal injury. This figure is an illustration of the dendrograms shown in Figures 8A-B.

Figure 4 depicts the gene expression is changed in a timely dependent fashion with multiple trends. The RRR differential gene expressions clustered into 27 trends in a timely dependent fashion, three of which were singletons (supplemented Fig 10). Here are presented 6 major trends: (A) Trend 5, exhibited 190 genes that were consistently up-regulated from the first day and were still up-regulated at two weeks. These genes involved in the defense response, ECM, cell growth and cell communication; (B) Trend 2, exhibited 194 genes that were up-regulated till the second RRR day, after which the expression started to decline. It includes genes of ribosome, cell death, RNA binding, response to abiotic stimulus, enzyme binding and regulation of cell cycle; (C) Trend 4, exhibited 34 genes that peaked on the second RRR, after which the expression decreased back to normal levels. These included genes as ribosomal genes RNA binding, metabolism, intracellular and translational elongation; (D) Trend 1, exhibited 230 genes down regulated genes from the first day and were still down-regulated at two weeks, many of which involved in metabolism and catabolism. (E) Trend 16, exhibited 87 down-regulated genes till the 5<sup>th</sup> day RRR, where it got back to normal levels. These included genes as calcium ion homeostasis, cell growth and/or maintenance, metal ion homeostasis, cell adhesion and positive regulation of cell proliferation (F) Trend 11, exhibited 46 down-regulated genes till the 5<sup>th</sup> day RRR, where it started to get back to normal levels. These genes involved in the ion transporter activity, mitochondria. See table 9 for information on the genes and the trends. The data is presented in fold ratios from the normal genes expression.

Figure 5 depicts the differentially expressed genes in RRR and RCC are regulated similarly. Of the genes whose expression was profiled, 984 genes, printed on the array, were previously described to be differentially expressed in RCC from normal kidney. These genes were qualitatively crossed compared with the current microarray study identifying 1325 RRR differentially expressed genes from normal kidney. 361 genes are expressed in both RRR and RCC (A), 278 concordantly expressed genes and 83 discordantly expressed genes. The data is presented in van diagrams (B). The p value is  $p < 0.05$

Figure 6 depicts the differentially expressed genes found in both RRR and RCC exhibited distinct ontologies for concordance and discordance expressed genes and pathways. The functional ontology (Fisher Exact  $p < 0.05$ ) of the differentially expressed genes in both RRR and RCC were crossed compared relative to their expression: concordantly, discordantly,

oxygenation and pathways: renal cell culture hypoxia responsive genes vs. normoxia; HIF regulated genes (HRE); VHL, IGF, MYC, NF-kB pathway genes; purine pathway genes; gene expression following renal ischemia reperfusion and/or acute renal failure (ARF) v. normal tissue (A); enlarged are presented ontologies of discordantly expressed genes (B); and  
 5 discordantly expressed genes (C).

Figure 7 depicts a molecular interaction map of the RRR- RCC-related pathways in which gene expression differences were observed. A, molecular interaction map. B, summary of symbol definitions. (See Kohn 1999). Although the symbol definitions are independent of color, we have adopted the following color convention to improve clarity. Red, inhibitory  
 10 interaction; green, stimulatory interaction; purple, transcriptional stimulation; black, binding interaction.

Figure 8 depicts the RRR gene expression signature defined three large subsets of early, late and continuously changed genes. A total of 39 kidneys (normal, ischemic, immediately following ischemia and RRR for 1, 2, 5 and 14 days) were each analyzed  
 15 separately on a microarray. The samples clustered into: early RRR differentially expressed genes at days 1 and 2 (A) and late 5 and 14 days (B). The joined cluster was maintained and illustrated in Figure 3.

Figure 9 depicts differentially expressed genes were validated by QPCR. The expression of the genes HIF-prolyl hydroxylase 1. 2 and 3 (egln2, egln1 and egln3  
 20 respectively) was validated by QPCR. The expression is up-regulated in normal kidney and down-regulated in regenerating kidney.

Figure 10 depicts the differential gene expressions clustered into 27 trends. The differential gene expressions clustered into 27 trends in a timely dependent fashion, three of which were singletons. In the first set, the cluster of the 27 trends is shown. That is the  
 25 expression of each gene is plotted.

Figure 11 depicts the differential gene expressions clustered into 27 trends. The 27 trends are the average differential gene expression of the clusters shown in Figure 10. The data is presented in fold ratios from the normal genes expression. The identity of the genes in the trends is available in Table 9.

Figure 12 depicts temporal patterns of gene expression during RRR. A. Principal component analysis of gene expression data during RRR. The first two principal components, PC-1 and PC-2, explain 22.2% and 12.1% of the total variance, respectively. B. The RRR gene expression distribution: 23% of the genes were differentially expressed. The differential

gene expression is presented here as up or down in regenerating, as opposed normal or ischemic kidney.

Figure 13 The differentially expressed genes were clustered according to their pattern of expression as early, late or continually RRR. Functional ontology was analysis performed (p<0.05). The presented ontologies are the ontology core and are hyperlinked to EMBL-EBI. The average RRR expression (log2) of each ontology is presented in a green to red scale; green down-regulated, red up-regulated. The numbers and average RRR expression of up- and down-regulated genes, the category p-value and enrichment are shown as well. Differentially expressed genes were validated by QPCR. The gene expression of IGFBP1, IGFBP 3, CTGF, AKT, FRAP, MYC, NF-kB, HK1, SIRT7, PHD1, was validated by QPCR. The gene expression of PHD2 and PHD3 was quantified as well

#### DETAILED DESCRIPTION OF THE INVENTION

We describe herein, *inter alia*, novel methods for accurately and quickly diagnosing and monitoring the tissue status, for example renal status. Also described herein are novel methods of screening for drug candidates and for treating patients suffering from cancer or organ injury or subject to organ transplantation.

As described herein, extensive molecular and bioinformatics analysis of renal regeneration and repair in a C57BL/6 mouse model and in human renal carcinoma were done. The analysis of the renal regeneration gene expression signature uncovered three patterns characterized by differential gene expression patterns occurring either early, late, or continuously during kidney regeneration, thereby revealing the complexity of the wound-healing process. Comparison of this gene expression profile with the profile of renal cell carcinoma (RCC) reported in the literature revealed a substantial concordance between the biology of renal regeneration and RCC pathogenesis. The identified discordant pattern differentiating the two processes are useful for identifying cells that are in the process of malignant transformation.

Based on the comparative analysis of these concordant and discordant gene expression patterns, we have identified gene expression programs of pathways, functions, and cellular locations that appear to play a multifaceted role in wound healing and/or carcinogenesis.

The introduction of microarray technology has enabled the characterization and comparison of global gene expression signatures of regenerating and malignant tissues. Recent microarray studies comparing wounds and tumors have provided molecular evidence that

keratinocytes at wound margins have gene expression profiles similar to that of squamous cell carcinoma (Pedersen TX et al. 2003). The Brown laboratory at Stanford has recently published a novel *in-vitro* study characterizing the changes in the global gene-expression profile of fibroblasts exposed to serum, and compared the results with publicly available gene expression data for numerous tumors. The study provides further evidence that a close similarity between the gene expression profile of fibroblasts involved in wound healing process and that characteristic of tumorigenesis exists (Chang HY et al 2004, Grose R. 2004). Our present study extends these observations to renal regeneration and renal carcinoma, but also for first time examines comprehensively the differences between these two processes.

Kidney is a member of a restricted class of organs capable of regeneration and repair following traumatic events such as ischemia/reperfusion injury, which is the major cause of acute renal failure (ARF) in both native (Rabb H and Martin JG 1997) and transplanted kidney (Shoskes DA, and Halloran PF (1996)). In the majority of cases of non-chronic ARF, kidney tissue regenerates and regains complete functionality in the absence of persistent inflammation and fibrosis, even when the initial injury and functional decline are very pronounced (Ysebaert DK et al 2004). The process of renal regeneration and repair (RRR) begins shortly after injury, a period during which necrotic cells are accompanied by replicating cells lining the injured proximal renal tubule. The commitment to DNA synthesis in this population of proliferating cells occurs rapidly, temporally coinciding with the emergence of morphologic and functional derangements. Ischemia/reperfusion injury, regeneration and recovery are part of the same continuum of biological responses and depend on the coordination of the cell-cycle machinery as well as the cells' ability to survive the initial injury (Price PM et al 2004). Clinically and biologically, ischemic ARF is a complex but orderly continuum that can be separated into a series of four overlapping phases that have been referred to as "initiation," "extension," "maintenance," and "recovery" (Sutton TA et al 2002).

Renal cell carcinoma (RCC) accounts for 3% of all adult male malignancies in the United State (Jemal A. et al 2004) and is a clinicopathologically heterogeneous disease that includes several histologically distinct cellular subtypes. A majority of the published evidence suggests that proximal renal tubules are the sites from which malignant RCC cells originate, although a recent study offers evidence that such cells may also originate from distal tubules (Motzer RJ et al 1996; Mandriota SJ et al 2002). A number of genetic syndromes predispose to the development of RCC, and genes associated with five of these syndromes have been identified: von Hippel-Lindau (VHL), met proto-oncogene (MET), fumarate hydratase (FH), Birt-Hgg-Dube syndrome (BHD) and hyperparathyroidism 2 (HRPT2) (Pavlovich and

Schmidt 2004). RCC also frequently develops in conjunction with polycystic kidney disease and renal allografts, both of which conditions induce a chronic regenerative response (Brennan et al 1991, Gomez Garcia I et al 2004).

The present invention is based upon the discovery that relative to the normal kidney, certain markers are differentially present in samples of renal cancer and in kidney recovering from ischemia and are grouped into two distinct signatures: (1) a substantial concordant overlap reflecting the normal regenerative phenotype, and (2) a divergent discordant (inverted) pattern of expression where gene expression changes are in opposite direction in renal cancer and in kidney recovering from ischemia. Accordingly, the amount of one or more markers found in a test sample compared to a kidney recovering from ischemia, or the presence or absence of one or more markers in the test sample provides useful diagnostic and therapeutic information regarding the renal status of the patient.

### Definitions

The "initiation phase," as used herein, refers to the beginning of ischemic ARF. This occurs when renal blood flow decreases to a level resulting in severe cellular ATP depletion, which in turn leads to acute tubular epithelial cell injury and dysfunction of the normal framework of filamentous actin (F-actin) in the cell. Usually, these alterations fall short of being lethal to the cell, but they disrupt the ability of renal tubular epithelial cells and renal vascular endothelial cells to maintain normal renal function. Additionally, the structural abnormalities observed in the renal vasculature during ischemic ARF can be attributed to the ischemic injury to vascular smooth muscle cells and endothelial cells. The inflammatory cascade is initiated in this pattern, possibly by the up-regulation of a variety of chemokines and cytokines that includes IL-1, IL-6, IL-8, monocyte chemoattractant protein-1 (MCP-1), and TNF-alpha. The transcription factor NF-kB is also reported to be up-regulated in the "initiation" phase (Sutton TA et al 2002).

The "extension phase," as used herein, is ushered in by two major events: continued hypoxia following the initial ischemic event and an inflammatory response. During this phase, cells continue to undergo injury and death, with both necrosis and apoptosis occurring predominantly in the outer medulla. In contrast, the proximal tubule cells of the outer cortex, where blood flow has returned to near-normal levels, undergo cellular repair and improve morphologically. As cellular injury continues in the medullary region during the extension pattern, the glomerular filtration rate continues to fall. There is continued production and release of chemokines and cytokines that further enhance the inflammatory cascade. Based on animal models of renal ischemia, inflammatory cell infiltration in the outer medullary region

of the kidney is evident as early as two hours after ischemic injury and is pronounced by 24 hours after the event (Sutton TA et al 2002).

As used herein, "maintenance phase," refers to the phase when cells undergo repair or apoptosis, proliferate, acquire the ability to migrate, and synthesize ECM proteins to re-establish and maintain the structural integrity of cells and tubules. The glomerular filtration rate becomes stabilized, albeit at a level determined by the severity of the initial traumatic event. This cellular repair and reorganization pattern results in slowly improving cellular function and sets the stage for improvement in organ function. Blood flow approaches normal, and epithelial cells establish intracellular and intercellular homeostasis (Sutton TA et al). During the final "recovery phase" of RRR, cellular differentiation continues, epithelial polarity is re-established, and normal cellular and organ function returns (Sutton TA et al 2002).

Unless defined otherwise, all technical and scientific terms used herein have the meaning commonly understood by a person skilled in the art to which this invention belongs. The following references provide one of skill with a general definition of many of the terms used in this invention: Singleton *et al.*, *Dictionary of Microbiology and Molecular Biology* (2nd ed. 1994); *The Cambridge Dictionary of Science and Technology* (Walker ed., 1988); *The Glossary of Genetics*, 5th Ed., R. Rieger *et al.* (eds.), Springer Verlag (1991); and Hale & Marham, *The Harper Collins Dictionary of Biology* (1991). As used herein, the following terms have the meanings ascribed to them unless specified otherwise.

The term "tissue status" refers to the histological status of a tissue sample. For example, diseases state or injury state of the tissue.

The term "renal status" refers to the status of the kidney tissue in a subject. Examples of types of renal statuses include, but are not limited to, the subject's risk of cancer, acute renal failure, the presence or absence of disease, the stage of disease in a patient, and the effectiveness of treatment of disease. Other statuses and degrees of each status are known in the art.

The term "sample" refers to cells, tissue samples or cell components (such as cellular membranes or cellular components) obtained from the treated subject. By one embodiment the sample are cells known to manifest the disease, for example, where the disease is cancer of type X, the cells are the cells of the tissue of the cancer (kidney, etc.) or metastasis of the above. By another embodiment the sample may be non-diseased cells such as cells obtained from a non-involved breast or other tissue.

The sample may be taken from biopsy, a bodily fluid, such as blood, lymph fluid, ascites, serous fluid, pleural effusion, sputum, cerebrospinal fluid, lacrimal fluid, synovial fluid, saliva, stool, sperm and urine. The sample may also originate from a tissue, such as brain, lung, liver, spleen, kidney, pancreas, intestine, colon, mammary gland or kidney, stomach, prostate, bladder, placenta, uterus, ovary, endometrium, testicle, lymph node, skin, head or neck, esophagus, bone marrow, and blood or blood cells. Cells suspected of being transformed may be obtained by methods known for obtaining "suspicious" cells such as by biopsy, needle biopsy, fine needle aspiration, swabbing, surgical excision, and other techniques known in the art. A sample may be tissue samples or cell from a subject, for example, obtained by biopsy, intact cells, for example cell that have been separated from a tissue sample, or intact cells present in blood or other body fluid, cells or tissue samples obtained from the subject, including paraffin embedded tissue samples, proteins extracted obtained from a cell, cell membrane, nucleus or any other cellular component or mRNA obtained from the nucleus or cytosol. As used herein, the "cell from the subject" may be one or more of a renal cell carcinoma, cyst, cortical tubule, ischemic tissue, regenerative tissue, or any histological or cytological stage in-between. The cells are sometimes herein referred to as a sample.

"Probe" in the context of this invention refers to a device adapted to engage a probe interface of a gas phase ion spectrometer (e.g., a mass spectrometer) and to present an analyte to ionizing energy for ionization and introduction into a gas phase ion spectrometer, such as a mass spectrometer. A "probe" will generally comprise a solid substrate (either flexible or rigid) comprising a sample presenting surface on which an analyte is presented to the source of ionizing energy.

"Adsorption" refers to detectable non-covalent binding of an analyte to an adsorbent or capture reagent.

"Eluant" or "wash solution" refers to an agent, typically a solution, which is used to affect or modify adsorption of an analyte to an adsorbent surface and/or remove unbound materials from the surface. The elution characteristics of an eluant can depend, for example, on pH, ionic strength, hydrophobicity, degree of chaotropism, detergent strength and temperature.

"Analyte" refers to any component of a sample that is desired to be detected. The term can refer to a single component or a plurality of components in the sample.



"Molecular binding partners" and "specific binding partners" refer to pairs of molecules, typically pairs of biomolecules that exhibit specific binding. Molecular binding partners include, without limitation, receptor and ligand, antibody and antigen, biotin and avidin, and biotin and streptavidin.

5 "Monitoring" refers to recording changes in a continuously varying parameter.

"Biochip" refers to a solid substrate having a generally planar surface to which an adsorbent is attached. Frequently, the surface of the biochip comprises a plurality of addressable locations, each of which location has the adsorbent bound there. Biochips can be adapted to engage a probe interface and, therefore, function as probes.

10 "Protein biochip" refers to a biochip adapted for the capture of polypeptides. Many protein biochips are described in the art. These include, for example, protein biochips produced by CIPHERGEN Biosystems (Fremont, CA), Packard BioScience Company (Meriden CT), Zyomix (Hayward, CA) and Phyllos (Lexington, MA). Examples of such protein biochips are described in the following patents or patent applications: U.S. patent 6,225,047  
15 (Hutchens and Yip, "Use of retentate chromatography to generate difference maps," May 1, 2001); International publication WO 99/51773 (Kuimelis and Wagner, "Addressable protein arrays," October 14, 1999); U.S. patent 6,329,209 (Wagner et al., "Arrays of protein-capture agents and methods of use thereof," December 11, 2001) and International publication WO 00/56934 (Englert et al., "Continuous porous matrix arrays," September 28, 2000).

20 Optical methods of detection include, for example, detection of fluorescence, luminescence, chemiluminescence, absorbance, reflectance, transmittance, birefringence or refractive index (e.g., surface plasmon resonance, ellipsometry, a resonant mirror method, a grating coupler waveguide method or interferometry). Optical methods include microscopy (both confocal and non-confocal), imaging methods and non-imaging methods.

25 Immunoassays in various formats (e.g., ELISA) are popular methods for detection of analytes captured on a solid phase. Electrochemical methods include voltammetry and amperometry methods. Radio frequency methods include multipolar resonance spectroscopy.

The term "measuring" means methods which include detecting the presence or absence of marker(s) in the sample, quantifying the amount of marker(s) in the sample, and/or  
30 qualifying the type of biomarker. Measuring can be accomplished by methods known in the art and those further described herein, including but not limited to quantitative PCR, semi-quantitative PCR, reverse transcriptase PCR, real time PCR, real time reverse transcriptase PCR, in situ PCR, SELDI and immunoassay. For example, PCR may be done using Applied

Biosystems MicroFluidic Card. Any suitable methods can be used to detect and measure one or more of the markers described herein. These methods include, without limitation, mass spectrometry (e.g., laser desorption/ionization mass spectrometry), fluorescence (e.g. biochip reader, sandwich immunoassay), radio-isotope detection, surface plasmon resonance, ellipsometry and atomic force microscopy.

The phrases "differentially present" and "differentially expressed" refer to differences in the existence, quantity, incidence and/or frequency of a marker present in a sample taken from patients having human cancer as compared to a control subject. A marker can be a nucleic acid or a polypeptide which is detected at a higher frequency or at a lower frequency in samples of human cancer patients compared to samples of control subjects, e.g., a marker may not be present in a normal sample, but may be present in a cancerous sample. A marker can be differentially present in terms of quantity, frequency, existence or incidence, or a combination thereof.

A nucleic acid is differentially present between two samples if the amount of the nucleic acid in one sample is statistically significantly different from the amount of the nucleic acid in the other sample. For example, a nucleic acid is differentially present between the two samples if it is present at least about 120%, at least about 130%, at least about 150%, at least about 180%, at least about 200%, at least about 300%, at least about 500%, at least about 700%, at least about 900%, or at least about 1000% greater than it is present in the other sample, or if it is detectable in one sample and not detectable in the other.

A biomarker (also referred to herein as a "marker") is an organic biomolecule which is differentially present in a sample taken from a subject of one phenotypic status (e.g., having a disease) as compared with another phenotypic status (e.g., not having the disease). A biomarker is differentially present between different phenotypic statuses if the mean or median expression level of the biomarker in the different groups is calculated to be statistically significant. Common tests for statistical significance include, among others, t-test, ANOVA, Kruskal-Wallis, Wilcoxon, Mann-Whitney and odds ratio. Biomarkers, alone or in combination, provide measures of relative risk that a subject belongs to one phenotypic status or another. Therefore, they are useful as markers for disease (diagnostics), therapeutic effectiveness of a drug (theranostics) and drug toxicity.

Alternatively or additionally, a nucleic acid is differentially present between two sets of samples if the frequency of detecting the nucleic acid in the renal cancer patients' samples is statistically significantly higher or lower than in the control samples. For example, a nucleic acid is differentially present between the two sets of samples if it is detected at least

about 120%, at least about 130%, at least about 150%, at least about 180%, at least about 200%, at least about 300%, at least about 500%, at least about 700%, at least about 900%, or at least about 1000% more frequently or less frequently observed in one set of samples than the other set of samples.

5           A “test amount” of a marker refers to an amount of a marker present in a sample being tested. A test amount can be either in absolute amount (*e.g.*,  $\mu\text{g/ml}$ ) or a relative amount (*e.g.*, relative intensity of signals).

          A “diagnostic amount” of a marker refers to an amount of a marker in a subject’s sample that is consistent with a diagnosis of renal cancer or kidney recovering from ischemia.

10          A diagnostic amount can be either in absolute amount (*e.g.*,  $\mu\text{g/ml}$ ) or a relative amount (*e.g.*, relative intensity of signals).

          A “control amount” of a marker can be any amount or a range of amount, which is to be compared against a test amount of a marker. For example, a control amount of a marker can be the amount of a marker in a person without renal cancer, a person with ischemic injury,  
15          or a primary culture cell line or an established cell line. A control amount can be either in absolute amount (*e.g.*,  $\mu\text{g/ml}$ ) or a relative amount (*e.g.*, relative intensity of signals).

          “Antibody” refers to a polypeptide ligand substantially encoded by an immunoglobulin gene or immunoglobulin genes, or fragments thereof, which specifically binds and recognizes an epitope (*e.g.*, an antigen). The recognized immunoglobulin genes  
20          include the kappa and lambda light chain constant region genes, the alpha, gamma, delta, epsilon and mu heavy chain constant region genes, and the myriad immunoglobulin variable region genes. Antibodies exist, *e.g.*, as intact immunoglobulins or as a number of well-characterized fragments produced by digestion with various peptidases. This includes, *e.g.*, Fab’ and F(ab’)<sub>2</sub> fragments. The term “antibody,” as used herein, also includes antibody  
25          fragments either produced by the modification of whole antibodies or those synthesized de novo using recombinant DNA methodologies. It also includes polyclonal antibodies, monoclonal antibodies, chimeric antibodies, humanized antibodies, or single chain antibodies. “Fc” portion of an antibody refers to that portion of an immunoglobulin heavy chain that comprises one or more heavy chain constant region domains, CH<sub>1</sub>, CH<sub>2</sub> and CH<sub>3</sub>, but does not  
30          include the heavy chain variable region.

          “Managing treatment” refers to the behavior of the clinician or physician subsequent to the determination of renal status. For example, if the result of the methods of the present invention is inconclusive or there is reason that confirmation of status is necessary, the

physician may order more tests. Alternatively, if the status indicates that surgery is appropriate, the physician may schedule the patient for surgery. Likewise, if the status is negative, e.g., late stage renal cancer or if the status is acute, no further action may be warranted. Furthermore, if the results show that treatment has been successful, no further management may be necessary.

As used herein, the term "assessing" and "analyzing" are intended to include quantitative and qualitative determination in the sense of obtaining an absolute value for the amount or concentration of the analyte present in the sample, and also of obtaining an index, ratio, percentage, visual and/or other value indicative of the level of analyte in the sample. Assessment may be direct or indirect and the chemical species actually detected need not of course be the analyte itself but may for example be a derivative thereof or some further substance.

The term "modulated" refers to changes in of one or more of the parameters, e.g., the expression of a marker or the level of the expression of a marker.

As used herein, "related clinical intervention" includes chemoprevention and surgical intervention.

"A tumor that responds" refers to a change in the tumor as a result of a treatment, for example, a reduction or stability in growth or invasive potential of the tumor, e.g., a favorable response. A tumor is also considered to respond if it increases or if it becomes more unstable, or exhibits metastasis.

The method may further comprise reporting the expression profile of the marker or markers or the correlations of the expression profiles thereof to the subject or a health care professional. This may be done as a "raw" results that has not been correlated, e.g., as a report of just the determined parameters, or it may be a correlated result.

"Diagnostic," "diagnosing," and the like refer to identifying the presence or nature of a pathologic condition, i.e., renal cancer. Diagnostic methods differ in their sensitivity and specificity. The "sensitivity" of a diagnostic assay is the percentage of diseased individuals who test positive (percent of "true positives"). Diseased individuals not detected by the assay are "false negatives." Subjects who are not diseased and who test negative in the assay, are termed "true negatives." The "specificity" of a diagnostic assay is 1 minus the false positive rate, where the "false positive" rate is defined as the proportion of those without the disease who test positive. While a particular diagnostic method may not provide a definitive diagnosis of a condition, it suffices if the method provides a positive indication that aids in diagnosis.

The terms "subject" or "patient" are used interchangeably herein, and is meant a mammalian subject to be treated, with human subjects being preferred. In some cases, the methods of the invention find use in experimental animals, in veterinary application, and in the development of animal models for disease, including, but not limited to, rodents including mice, cows, rats, and hamsters, primates, pigs, horses, chickens, cats, or dogs and the like.

The cell from the subject suspected of being cancerous may be anywhere along the progression from normal to neoplastic, including metastatic. For example, such a cell is not normal, and may exhibit signs of dysplasia, or any other pathology between, and including, normal and neoplasia.

The terms "reverse transcription polymerase chain reaction" and "RT-PCR" refer to a method for reverse transcription of an RNA sequence to generate a mixture of cDNA sequences, followed by increasing the concentration of a desired segment of the transcribed cDNA sequences in the mixture without cloning or purification. Typically, RNA is reverse transcribed using a single primer (e.g., an oligo-dT primer) prior to PCR amplification of the desired segment of the transcribed DNA using two primers.

The term "polynucleotide" as used herein refers to a polymeric molecule having a backbone that supports bases capable of hydrogen bonding to typical polynucleotides, where the polymer backbone presents the bases in a manner to permit such hydrogen bonding in a sequence specific fashion between the polymeric molecule and a typical polynucleotide (e.g., single-stranded DNA). Such bases are typically inosine, adenosine, guanosine, cytosine, uracil and thymidine. Polymeric molecules include double and single stranded RNA and DNA, and backbone modifications thereof, for example, methylphosphonate linkages.

As used herein, the term "primer" refers to an oligonucleotide, whether occurring naturally as in a purified restriction digest or produced synthetically, which is capable of acting as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product which is complementary to a nucleic acid strand is induced, (i.e., in the presence of nucleotides and of an inducing agent such as DNA polymerase and at a suitable temperature and pH). The primer is preferably single stranded for maximum efficiency in amplification, but may alternatively be double stranded. If double stranded, the primer is first treated to separate its strands before being used to prepare extension products. Preferably, the primer is an oligodeoxyribonucleotide. The primer must be sufficiently long to prime the synthesis of extension products in the presence of the inducing agent. The exact lengths of the primers will depend on many factors, including temperature, source of primer and the use of the method.

When determining the levels of transcripts, the transcripts may have the published sequences, or they may be substantially identical to the published sequences due to polymorphisms or mutations.

As used herein, "substantial sequence identity" in the nucleic acid sequence comparison context means either that the segments, or their complementary strands, when compared, are identical when optimally aligned, with appropriate nucleotide insertions or deletions, in at least about 50% of the nucleotides, generally at least 56%, more generally at least 59%, ordinarily at least 62%, more ordinarily at least 65%, often at least 68%, more often at least 71%, typically at least 74%, more typically at least 77%, usually at least 80%, more usually at least about 85%, preferably at least about 90%, more preferably at least about 95 to 98% or more, and in particular embodiments, as high at about 99% or more of the nucleotides. Alternatively, substantial sequence identity exists when the segments will hybridize under selective hybridization conditions, to a strand, or its complement, typically using a fragment derived from the sequences. Typically, selective hybridization will occur when there is at least about 55% sequence identity over a stretch of at least about 14 nucleotides, preferably at least about 65%, more preferably at least about 75%, and most preferably at least about 90%. See Kanehisa (1984) *Nuc. Acids Res.* 12:203-213. The length of sequence identity comparison, as described, may be over longer stretches, and in certain embodiments will be over a stretch of at least about 17 nucleotides, usually at least about 20 nucleotides, more usually at least about 24 nucleotides, typically at least about 28 nucleotides, more typically at least about 40 nucleotides, preferably at least about 50 nucleotides, and more preferably at least about 75 to 100 or more nucleotides. The endpoints of the segments may be at many different pair combinations. In determining sequence identity or percent homology the below discussed protocols and programs for sequence similarity are suitably employed including the BLAST algorithm.

The term "polymorphism" refers to the coexistence of more than one form of a gene or portion (e.g., allelic variant) thereof. A portion of a gene of which there are at least two different forms, i.e., two different nucleotide sequences, is referred to as a "polymorphic region of a gene". A specific genetic sequence at a polymorphic region of a gene is an allele.

A polymorphic region can be a single nucleotide, the identity of which differs in different alleles. A polymorphic region can also be several nucleotides long. The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against public databases to identify, for example, other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST

programs (version 2.0) of Altschul, et al. (1990) J. Mol. Biol. 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to the genes listed on table 15 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to NIP2b, NIP2cL, and NIP2cS protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) Nucleic Acids Res. 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See  
10 <http://www.ncbi.nlm.nih.gov>.

Sequence identity searches can be also performed manually or by using several available computer programs known to those skilled in the art. Preferably, Blast and Smith-Waterman algorithms, which are available and known to those skilled in the art, and the like can be used. Blast is NCBI's sequence similarity search tool designed to support analysis of  
15 nucleotide and protein sequence databases. The GCG Package provides a local version of Blast that can be used either with public domain databases or with any locally available searchable database. GCG Package v9.0 is a commercially available software package that contains over 100 interrelated software programs that enables analysis of sequences by editing, mapping, comparing and aligning them. Other programs included in the GCG  
20 Package include, for example, programs which facilitate RNA secondary structure predictions, nucleic acid fragment assembly, and evolutionary analysis. In addition, the most prominent genetic databases (GenBank, EMBL, PIR, and SWISS-PROT) are distributed along with the GCG Package and are fully accessible with the database searching and manipulation programs. GCG can be accessed through the Internet at, for example, <http://www.gcg.com/>.  
25 Fetch is a tool available in GCG that can get annotated GenBank records based on accession numbers and is similar to Entrez. Another sequence similarity search can be performed with GeneWorld and GeneThesaurus from Pangea. GeneWorld 2.5 is an automated, flexible, high-throughput application for analysis of polynucleotide and protein sequences. GeneWorld allows for automatic analysis and annotations of sequences. Like GCG, GeneWorld  
30 incorporates several tools for sequence identity searching, gene finding, multiple sequence alignment, secondary structure prediction, and motif identification. GeneThesaurus 1.0™ is a sequence and annotation data subscription service providing information from multiple sources, providing a relational data model for public and local data.

Another alternative sequence identity search can be performed, for example, by BlastParse. BlastParse is a PERL script running on a UNIX platform that automates the strategy described above. BlastParse takes a list of biomarker accession numbers of interest and parses all the GenBank fields into "tab-delimited" text that can then be saved in a "relational database" format for easier search and analysis, which provides flexibility. The end result is a series of completely parsed GenBank records that can be easily sorted, filtered, and queried against, as well as an annotations-relational database.

As used herein, the term "specifically hybridizes" or "specifically detects" refers to the ability of a nucleic acid molecule to hybridize to at least approximately 6 consecutive nucleotides of a sample nucleic acid.

"Substantially purified" refers to nucleic acid molecules or proteins that are removed from their natural environment and are isolated or separated, and are at least about 60% free, preferably about 75% free, and most preferably about 90% free, from other components with which they are naturally associated.

As used herein, "variant" of polypeptides refers to an amino acid sequence that is altered by one or more amino acid residues. The variant may have "conservative" changes, wherein a substituted amino acid has similar structural or chemical properties (e.g., replacement of leucine with isoleucine). More rarely, a variant may have "nonconservative" changes (e.g., replacement of glycine with tryptophan). Analogous minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which amino acid residues may be substituted, inserted, or deleted without abolishing biological activity may be found using computer programs well known in the art, for example, LASERGENE software (DNASTAR).

A nucleic acid derived from a biomarker is one derived from at least the C-terminal 100 nucleic acids, 75 nucleic acids, 50 nucleic acids, 25 nucleic acids, 10 nucleic acids, or 5 nucleic acids. Alternately, the isolated nucleic acid has a sequence corresponding to the amino acid sequence as identified by the sequences, or fragments or variants thereof. Nucleic acids of the invention may be at least about 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99.9% identical to the nucleotide sequence identified by the sequences, fragments or variants thereof, or one that is identified in a screening assay described herein. Nucleic acids may also be those capable of encoding a polypeptide having substantial sequence identity to the sequence identified by the sequences, fragments or variant thereof, and characterized by the ability to alter the expression pattern of a biomarker. Nucleic acids of the invention may be at least about 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99.9% identical to the nucleic acids capable



of encoding a polypeptide having substantial sequence identity to those identified by the screening assays described herein, fragments or variant thereof, and characterized by the ability to alter the expression pattern of a biomarker.

An isolated polypeptide, of the invention, may be a peptide derived from a biomarker, wherein the polypeptide stimulates an alternation in the subcellular expression pattern of a biomarker. The peptide may be an amino acid sequence as identified by the sequences, or fragments or variants thereof. The peptide is at least about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% identical to any one or more of the amino acid sequences identified by the sequences. The peptide may also be a peptide identified by the screening methods described herein or fragments or variants thereof. For example, the peptide may be a peptide that is at least about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% identical to any one or more of the amino acid sequences identified by a screening method described herein.

As used herein, the term "an oligonucleotide having a nucleotide sequence encoding a gene" means a nucleic acid sequence comprising the coding region of a gene, i.e. the nucleic acid sequence which encodes a gene product. For example, the the sequences is an oligonucleotide encoding a c-terminal portion of the a biomarker gene. The coding region may be present in either a cDNA, genomic DNA or RNA form. When present in a DNA form, the oligonucleotide may be single-stranded (e.g., the sense strand) or double-stranded. Suitable control elements such as enhancers, promoters, splice junctions, polyadenylation signals, etc. may be placed in close proximity to the coding region of the gene if needed to permit proper initiation of transcription and/or correct processing of the primary RNA transcript. Alternatively, the coding region utilized in the expression vectors of the present invention may contain endogenous enhancers, splice junctions, intervening sequences, polyadenylation signals, etc. or a combination of both endogenous and exogenous control elements.

The terms "protein" and "polypeptide" are used interchangeably herein. The term "peptide" is used herein to refer to a chain of two or more amino acids or amino acid analogs (including non-naturally occurring amino acids), with adjacent amino acids joined by peptide (-NHCO-) bonds. Thus, the peptides of the invention include oligopeptides, polypeptides, proteins, mimetopes and peptidomimetics. Methods for preparing mimetopes and peptidomimetics are known in the art.

The terms "mimetope" and "peptidomimetic" are used interchangeably herein. A "mimetope" of a compound X refers to a compound in which chemical structures of X necessary for functional activity of X have been replaced with other chemical structures which

mimic the conformation of X. Examples of peptidomimetics include peptidic compounds in which the peptide backbone is substituted with one or more benzodiazepine molecules (see e.g., James, G.L. *et al.* (1993) *Science* 260:1937-1942) and “retro-inverso” peptides (see U.S. Patent No. 4,522,752 to Sisto). The terms “mimotope” and “peptidomimetic” also refer to a moiety, other than a naturally occurring amino acid, that conformationally and functionally serves as a substitute for a particular amino acid in a peptide-containing compound without adversely interfering to a significant extent with the function of the peptide. Examples of amino acid mimetics include D-amino acids. Peptides substituted with one or more D-amino acids may be made using well known peptide synthesis procedures. Additional substitutions include amino acid analogs having variant side chains with functional groups, for example, *l*-cyanoalanine, canavanine, djenkolic acid, norleucine, 3-phosphoserine, homoserine, etc.

“Discordant genes” refer to genes that are expressed in a divergent discordant (inverted) pattern of expression where gene expression changes are in opposite direction in cancer and normal tissue recovering from ischemia, by going through the processes of regeneration and repair, (e.g., kidney). Discordantly expressed genes include the genes labeled as discordantly expressed in Table 9. Discordant genes, as disclosed herein, are useful for diagnosing, treating or screening for candidate compounds to treat cancer and to aid in wound healing. For example, kidney cancer and wound healing (i.e. acute renal failure and kidney transplantation). The discordant pattern of expression could also be used to treat cancer and wound healing in brain, lung, liver, spleen, kidney, pancreas, intestine, colon, mammary gland or kidney, stomach, prostate, bladder, placenta, uterus, ovary, endometrium, testicle, lymph node, skin, head or neck, esophagus. It could also be used to treat cancer, metastasis, cyst, wound healing and ischemia of heart, lung, esophagus, bone, intestine, breast, brain, uterine cervix, testis, stomach, skin, and organs that are transplantable. For example, discordant gene expression patterns and signatures could be used to identify drugs that will slow the ischemia when shipping organs (e.g., live donors will be given drug and/or the transplanted organ will be treated with the same or different drugs). That is, divergent, discordant (inverted) pattern of expression is where gene expression changes are in the opposite direction in RRR and RCC. The RRR differential gene expression was qualitatively compared with the global gene expression of RCC as opposed to human normal kidney. Two distinct signatures were revealed: (1) a substantial concordant overlap reflecting the normal regenerative phenotype, and (2) a divergent discordant (inverted) pattern of expression where gene expression changes are in opposite direction in RRR and RCC. The RCC/normal tissue profile and the RRR/normal tissue profile was compared. Qualitative cross-comparison, e.g., “A”/“B” = RCC/RRR. The RCC/RRR produced two subgroups, e.g., concordant genes (up or

down regulated from normal in both RCC and RRR) and discordant genes (up regulated from normal in RCC and down regulated in RRR, or the other way round). Discordant genes can be used to diagnose and or treat cancer, wound healing, RRR, acute organ failure, organ transplantation.

“Clusters,” as used herein refer to patterns of gene expression that are similar. For example, three patterns of differentially expressed genes were categorized during days 1-14 of Renal Regeneration and Repair (RRR): continuous, early and late. “Trends,” refer to the averages of the identified clusters. The RRR differential gene expression as compared to normal kidney was further clustered to identify different temporal trends over the two-week period. We statistically identified 27 trends that are described in details in the supplemental material

BRB tools may be used to statistically identify clusters and trends. See <http://linus.nci.nih.gov/BRB-ArrayTools.html>.

“Gene Ontology (GO)” analysis can be done, for example, using the EASE software. Significant ontology for the three patterns of gene expression (continuous, early and late) were identified using EASE.

PubMed and other publicly available databases were searched to catalogue differentially regulated genes relative to the normal kidney/tissue for at least the following conditions or statuses: renal cell carcinoma (RCC), acute renal failure (ARF) and RRR, hypoxia, hypoxia inducible factor (HIF), (HIF binds to the Hypoxia Responsive Element (HRE) in the promoter of many genes), the VHL gene, the MYC gene, the p53 gene, the NF-kB gene, and the IGF gene. The datasets (catalogues) of the conditions or statuses were cross-compared with a microarray dataset of 1325 RRR genes. The significance of these cross-comparisons was also tested (x2 test).

“Concordant genes” refer to genes that reflect the normal regenerative phenotype. Concordant genes are up-regulated from normal in both RRR and RCC or down-regulated in both. Discordant genes are up-regulated from normal in RRR but down-regulated in RCC or the other way round. Concordant may also refer to genes or proteins differentially expressed in the same direction in RRR and RCC. Without wishing to be bound by any particular scientific theory, the concordant signatures qualitatively reflects the regenerative phenotype and discordant signatures reflect differences between malignancies and processes of tissue repair.

"Cosmetics" as used herein refer to ointments, powders, lotions, salves, and the like that are used by subjects on the skin. Compounds identified here can be added to cosmetics to treat wounds to the skin.

"Metastasis" as used herein indicates migrating tumor cells. The discordant and/or concordant gene profiles are useful for treating metastasis, e.g., renal metastasis and for screening for drugs to treat such metastasis.

"Renal cell carcinoma (RCC)" refers to a types of kidney cancer. Other kidney tumors are also included here, for example, Wilms tumors (WT), Birt-Hogg-Dube' (BHD), and hereditary papillary renal-cell carcinoma (HPRC).

## DESCRIPTION OF THE BIOMARKERS

**Concordant Biomarker: Mini-Chromosome Maintenance (Mcm2, 3, 4 and 7) And  
Discordant Biomarker: Vascular Endothelial Growth Factor (VEGF)**

One example of a marker that is useful in the methods of the present invention include the markers listed in one or more of Tables 7, 8, 9, 13, 20, and 23. The markers were detected by extensively surveying the literature and cataloging 2815 genes expressed differentially in RCC as relative to normal kidney. 984 of these genes were printed on the GEM2 array that we used for the RRR studies. Then RCC dataset was qualitatively cross-compared with the differential expression of the current set of 1,325 RRR genes as relative to normal kidney. The analysis revealed a group of 361 genes that matched both the experimental RRR dataset and the RCC literature. Of these 361 genes, 285 genes (77%) were concordantly expressed in both RRR and in RCC. The remainder of the 361 genes, 81 genes (23%), were discordantly expressed during RRR as compared to RCC. The protocols for isolating and identifying the markers described in one or more of Tables 7, 8, 9, 13, 20, and 23 and elsewhere herein are set forth below in the Examples.

A biomarker can be detected by any methodology. A preferred method for detection involves first capturing the biomarker, e.g., with biospecific capture reagents, and then detecting the captured biomarkers, e.g., nucleic acids with fluorescence detection methods or proteins by mass spectrometry. Preferably, the biospecific capture reagents are bound to a solid phase, such as a bead, a plate, a membrane or a chip. Methods of coupling biomolecules, such as nucleic acids and antibodies, to a solid phase are well known in the art. They can employ, for example, bifunctional linking agents, or the solid phase can be derivatized with a reactive group, such as an epoxide or an imidazole, that will bind the molecule on contact. Biospecific capture reagents against different target proteins can be mixed in the same place, or they can be attached to solid phases in different physical or addressable locations.

In yet another embodiment, the surfaces of biochips can be derivatized with the capture reagents in the same location or in physically different addressable locations. One advantage of capturing different markers in different addressable locations is that the analysis becomes simpler.

## 5 Types Of Sample And Preparation Of The Sample

The markers can be measured in different types of biological samples. The sample is preferably a biological cell or fluid sample. Examples of a biological cell samples include kidney cell, e.g., proximal renal tubule (PRT) cells, distal renal tubule (DRT) cells. Examples of a biological fluid sample useful in this invention include blood, blood serum, plasma, vaginal secretions, urine, tears, saliva, *etc.*

If desired, the sample can be prepared to enhance detectability of the markers. For example, the mRNA may be enriched in an RNA preparation from a cell sample. In fluid samples, such as a blood serum sample from the subject can be preferably fractionated by, e.g., Cibacron blue agarose chromatography and single stranded DNA affinity chromatography, anion exchange chromatography, affinity chromatography (e.g., with antibodies) and the like. The method of fractionation depends on the type of detection method used.

Any method that enriches for the nucleic acid or protein of interest can be used. Sample preparations, such as pre-fractionation protocols, are optional and may not be necessary to enhance detectability of markers depending on the methods of detection used. For example, sample preparation may be unnecessary if antibodies that specifically bind markers are used to detect the presence of markers in a sample.

Optionally, a marker can be modified before analysis to improve its resolution or to determine its identity. For example, the markers may be subject to proteolytic or endonuclease digestion before analysis. Any protease or endonuclease can be used. Proteases, such as trypsin, that are likely to cleave the markers into a discrete number of fragments are particularly useful.

## Data Analysis

When the sample is measured and data is generated, e.g., by mass spectrometry, the data is then analyzed by a computer software program. Generally, the software can comprise code that converts signal from the mass spectrometer into computer readable form. The software also can include code that applies an algorithm to the analysis of the signal to determine whether the signal represents a "peak" in the signal corresponding to a marker of

this invention, or other useful markers. The software also can include code that executes an algorithm that compares signal from a test sample to a typical signal characteristic of "normal" and human cancer and determines the closeness of fit between the two signals. The software also can include code indicating which the test sample is closest to, thereby providing a  
5 probable diagnosis.

In preferred methods of the present invention, multiple biomarkers are measured. The use of multiple biomarkers increases the predictive value of the test and provides greater utility in diagnosis, toxicology, patient stratification and patient monitoring. The process called "Pattern recognition" detects the patterns formed by multiple biomarkers greatly  
10 improves the sensitivity and specificity of clinical proteomics for predictive medicine. Subtle variations in data from clinical samples, e.g., obtained using SELDI, indicate that certain patterns of protein expression can predict phenotypes such as the presence or absence of a certain disease, a particular stage of cancer progression, or a positive or adverse response to drug treatments.

Baseline subtraction improves data quantification by eliminating artificial, reproducible instrument offsets that perturb the spectrum. Methods of subtracting baseline are well known in the art.

In one example, GenePix software, Axon Instruments, now part of Molecular Devices USA, is used to detect the results from the biochip. The data is classified using a pattern  
20 recognition process that uses a classification model. The statistical analysis was done on the statistical software BRB Arraytools developed by Dr. Richard Simon and Dr. Amy Peng Lam, NCI, NIH, USA. BRB ArrayTools is an integrated package for the visualization and statistical analysis of DNA microarray gene expression data. It was developed by professional statisticians experienced in the analysis of microarray data and involved in the development of  
25 improved methods for the design and analysis of microarray based experiments. The array tools package utilizes an Excel front end. Scientists are familiar with Excel and utilizing Excel as the front end makes the system portable and not tied to any database. The input data is assumed to be in the form of Excel spreadsheets describing the expression values and a spreadsheet providing user specified phenotypes for the samples arrayed. The analytic and  
30 visualization tools are integrated into Excel as an add-in. The analytic and visualization tools themselves are developed in the powerful R statistical system, in C and Fortran programs and in Java applications. Visual Basic for Applications is the glue that integrates the components and hides the complexity of the analytic methods from the user. The system incorporates a

variety of powerful analytic and visualization tools developed specifically for microarray data analysis.

Other software that were used are Microsoft Excel, FilemakerPro, Michael Eisen Cluster, EASE (Hosack DA et al 2003), GoMiner (Zeeberg BR et al 2003), Source (Diehn M. et al 2003) MatchMiner (Bussey et al 2003) and the p-value for the 2X2 table was calculated using Statistic Package R.

Classification models, e.g., to generate trends and clusters, can be formed using any suitable statistical classification (or "learning") method that attempts to segregate bodies of data into classes based on objective parameters present in the data. Classification methods may be either supervised or unsupervised. Examples of supervised and unsupervised classification processes are described in Jain, "Statistical Pattern Recognition: A Review", IEEE Transactions on Pattern Analysis and Machine Intelligence, Vol. 22, No. 1, January 2000, which is herein incorporated by reference in its entirety.

In supervised classification, training data containing examples of known categories are presented to a learning mechanism, which learns one more sets of relationships that define each of the known classes. New data may then be applied to the learning mechanism, which then classifies the new data using the learned relationships. Examples of supervised classification processes include linear regression processes (e.g., multiple linear regression (MLR), partial least squares (PLS) regression and principal components regression (PCR)), binary decision trees (e.g., recursive partitioning processes such as CART - classification and regression trees), artificial neural networks such as back propagation networks, discriminant analyses (e.g., Bayesian classifier or Fischer analysis), logistic classifiers, and support vector classifiers (support vector machines).

A preferred supervised classification method is a recursive partitioning process.

Recursive partitioning processes use recursive partitioning trees to classify spectra derived from unknown samples. Further details about recursive partitioning processes are provided in U.S. 2002 0138208 A1 (Pausle et al., "Method for analyzing mass spectra," September 26, 2002).

## Methods

Methods of determining the expression pattern of a polynucleotide in a sample are well known in the art and include, for example, RT-PCR analysis, in-situ hybridization and northern blotting; polynucleotide detection may also be performed by hybridizing a sample with a microarray imprinted with markers. Any other known methods of polynucleotide

detection are also envisaged in connection with the invention. Optimization of polynucleotide detection procedures for diagnosis is well known in the art and described herein below.

Specifically, diagnostic assays using the above methods are well known in the art (see, for example: Sidransky, "Nucleic Acid-Based methods for the Detection of Cancer", Science,

- 1997; 278: 1054-1058) and may be carried out essentially as follows: RT-PCR for diagnosis  
5 may be carried out essentially as described in Bernard & Wittwer, "Real-Time PCR Technology for Cancer Diagnostics", Clinical Chemistry 2002; 48(8): 1178-85; Raj et al., "Utilization of Polymerase Chain Reaction Technology in the Detection of Solid Tumors", Cancer 1998; 82(8): 1419-1442; Zippelius & Pantel, "RT-PCR-based detection of occult  
10 disseminated tumor cells in peripheral blood and bone marrow of patients with solid tumors. An overview", Ann NY Acad Sci 2000; 906:110-23. In-situ hybridization for diagnosis may be carried out essentially as described in "Introduction to Fluorescence In Situ Hybridization: Principles and Clinical Applications", Andreeff & Pinkel (Editors), John Wiley & Sons Inc., 1999; Cheung et al., "Interphase cytogenetic study of endometrial sarcoma by chromosome in  
15 situ hybridization, modern Pathology 1996; 9:910-918. Northern blotting for diagnosis may be carried out essentially as described in Trayhurn, "Northern blotting", Proc Nutr Soc 1996; 55(1B): 583-9; Shifman & Stein, "A reliable and sensitive method for non-radioactive Northern blot analysis of nerve growth factor mRNA from brain tissues", Journal of Neuroscience Methods 1995; 59: 205-208; Pacheco et al., "Prognostic significance of the  
20 combined expression of matrix metalloproteinase-9, urokinase type plasminogen activator and its receptor in renal cancer as measured by Northern blot analysis", Int J Biol Markers 2001; 16(1): 62-8. Polynucleotide microarray-based diagnosis can be carried out essentially as described in Ring & Boss, "Microarrays and molecular markers for tumor classification", Ucbaine Biol 2002; 3(5): comment 2005; Lacroix et al., "A low-density DNA microarray for  
25 analysis of markers in renal cancer", Int J Biol Markers 2002; 17(1): 5-23. In addition, polynucleotide microarray hybridization for diagnosis may be carried out essentially as described in the following review concerning micorarrays in the diagnosis of various cancers: Schmidt & Begley, "Cancer diagnosis and microarrays", The International Journal of Biochemistry and Cell Biology, 2003; 35: 119-124. Diagnostic assays using tissue microarrays  
30 are also possible and may be performed essentially as described in Ginestier et al., "Distinct and complementary information provided by use of tissue and DNA microarrays in the study of kidney tumor markers", Am J Pathol 2002; 161(4): 1223-33; Fejzo & Slamon, "Frozen tumor tissue microarray technology for analysis of tumor RNA, DNA and proteins", Am J Pathol 2001; 159(5): 1645-50.



An example of detection of polynucleotides in bodily fluid is that of expression profile determination or marker determination, which is diagnostic of the stage of a cancer by detection of the presence of specific cancer cells by RT-PCR of identified cancer-type-specific markers expression in the sample.

5 Any of the diagnostic methods as described above can also be used together, simultaneously or not, and can thus provide a stronger diagnostic tool and validate or strengthen the results of a particular diagnosis. For combinations of different diagnostic methods see, inter alia: Hoshi et al., "Enzyme-linked immunosorbent assay detection of prostate-specific antigen messenger ribonucleic acid in prostate cancer", *Urology* 1999; 53 (1): 228-235; Zhong-Ping et al., "Quantitation of ERCC-2 Gene Expression in Human Tumor Cell  
10 Lines by Reverse Transcription-Polymerase Chain Reaction in Comparison to Northern Blot Analysis", *Analytical Biochemistry* 1997; 244: 50-54; Hatta et al., "Polymerase chain reaction and immunohistochemistry frequently detect occult melanoma cells in regional lymph nodes of melanoma patients", *J Clin Pathol* 1998; 51(8): 597-601.

15 Methods of diagnosing a cancer in a subject comprise determining, in a sample from the subject, the expression profile at least one marker (nucleic acid or protein), wherein an expression pattern as identified in Table 9 is indicative of the renal status.

General protocols for the detection of cancer markers can be found in "Tumor Marker Protocols", Hanaussek & Walaszek (Eds.), Humana Press, 1998. Methods of determining the  
20 expression pattern of a polypeptide in a sample are well known in the art (see, for example: Coligan et al, Unit 9, *Current Protocols in Immunology*, Wiley Interscience, 1994) and include, inter alia: immunohistochemistry (*Microscopy, Immunohistochemistry and Antigen Retrieval Methods: For Light and Electron Microscopy*, M. A. Hayat (Author), Kluwer Academic Publishers, 2002; Brown C.: "Antigen retrieval methods for  
25 immunohistochemistry", *Toxicol Pathol* 1998; 26(6): 830-1; ELISA (Onorato et al., "Immunohistochemical and ELISA assays for biomarkers of oxidative stress in aging and disease", *Ann NY Acad Sci* 1998 20; 854: 277-90), western blotting (Laemmli UK: "Cleavage of structural proteins during the assembly of the head of a bacteriophage T4", *Nature* 1970;227: 680-685; Egger & Bienz, "Protein (western) blotting", *Mol Biotechnol*  
30 1994; 1(3): 289-305), antibody microarray hybridization (Huang, "detection of multiple proteins in an antibody-based protein microarray system, *Immunol Methods* 2001 1; 255 (1-2): 1-13) and Biomarkered molecular imaging, which can be carried out on the whole body with imaging agents such as antibodies against the marker polypeptides (which may be membrane-bound proteins), the marker polypeptides themselves, receptors and contrast

agents. The visualizations techniques include single photon and positron emission tomography, magnetic resonance imaging (MRI), computed tomography or ultrasonography (Thomas, Biomarkered Molecular Imaging in Oncology, Kim et al (Eds), Springer Verlag, 2001). Any other known methods of polypeptide detection are also envisaged in connection

5 with the invention. Optimization of protein detection procedures for diagnosis is well known in the art and described herein below. Specifically, diagnostic assays using the above methods may be carried out essentially as follows: Immunohistochemistry for diagnosis may be carried out essentially as described in Diagnostic Immunohistochemistry, David J., MD Dabbs, Churchill Livingstone, 1st Ed, 2002; Quantitative Immunohistochemistry: Theoretical

10 Background and its Application in Biology and Surgical Pathology, Fritz et al., Gustav Fischer, 1992. Western blotting-based diagnosis may be carried out essentially as described in Brys et al., "p53 protein detection by the Western blotting technique in normal and neoplastic specimens of human endometrium", Cancer Letters 2000; 148 (197-205); Rochon et al., "Western blot assay for prostate-specific membrane antigen in serum of prostate cancer

15 patients" Prostate 1994; 25(4): 219-23; Dalmau et al., "Detection of the anti-Hu antibody in the serum of patients with small cell lung cancer--a quantitative western blot analysis", Ann Neurol 1990; 27(5): 544-52; Joyce et al., "Detection of altered H-ras proteins in human tumors using western blot analysis", Lab Invest 1989; 61(2): 212-8. ELISA based diagnosis may be carried out essentially as described in D'ambrosio et al., "An enzyme-linked immunosorbent

20 assay (ELISA) for the detection and quantitation of the tumor marker 1-methylinosine in human urine", Clin Chim Acta 1991; 199(2): 119-28; Attalah et al., "A dipstick, dot-ELISA assay for the rapid and early detection of bladder cancer", Cancer Detect Prev 1991; 15(6): 495-9; Erdile et al., "Whole cell ELISA for detection of tumor antigen expression in tumor samples", Journal of Immunological Methods 2001; 258: 47-53. Antibody microarray-based

25 diagnosis may be carried out essentially as described in Huang, "detection of multiple proteins in an antibody-based protein microarray system, Immunol Methods 2001 1; 255 (1-2): 1-13. Biomarkered molecular imaging-based diagnosis may be carried out essentially as described in Thomas, Biomarkered Molecular Imaging in Oncology, Kim et al (Eds), Springer Verlag, 2001; Shahbazi-Gahruei et al., "In vitro studies of gadolinium-DTPA conjugated with

30 monoclonal antibodies as cancer-specific magnetic resonance imaging contrast agents", Australas Phys Eng Sci Med 2002; 25(1): 31-8; Tiefenauer et al., "Antibody-magnetite nanoparticles: in vitro characterization of a potential tumor-specific contrast agent for magnetic resonance imaging", Bioconjug Chem 1993; 4(5): 347-52; Cerdan et al., "Monoclonal antibody-coated magnetite particles as contrast agents in magnetic resonance

35 imaging of tumors", Magn Reson Med 1989; 12(2): 151-63. In addition, polypeptides may be

detected and a diagnostic assay performed using Mass Spectrometry, essentially as described in Bergquist et al., "peptide mapping of proteins in human body fluids using electrospray ionization fourier transform ion cyclotron resonance mass spectrometry", Mass Spectrometry Reviews, 2002; 21:2-15 and Gelpi, "Biomedical and biochemical applications of liquid-  
5 chromatography-mass spectrometry", Journal of Chromatography A, 1995; 703: 59-80.

The diagnostic methods of the invention as recited herein may also be employed to examine the status of a tumor cell or cells, or to examine the effectiveness of a modulator of the activity of a tumor cell, such as a drug. The examining may be by measuring the expression pattern of one or more of the transcripts and/or proteins listed in any one of Tables  
10 8 or 9. The drug may be any one or more of the drugs linked or generated by the software program and database as PharmaProjects and/or a compound or composition identified in a screening assay described herein.

A prognostic aspect of the invention provides a method of measuring the responsiveness of a subject to a cancer treatment comprising determining the expression  
15 profile of at least one marker in a sample taken from the subject before treatment, and comparing it with the expression profile of the marker in a sample taken from the subject after treatment. An expression pattern of a marker as listed in Table 9 indicating responsiveness of the subject to the cancer treatment, wherein the marker is selected from the group consisting of: markers listed in Table 9.

In addition, a prognostic aspect of the invention may further comprise methods of  
20 measuring the responsiveness of a subject to a cancer treatment comprising determining the expression profile of at least one transcript in a sample taken from the subject before treatment, and comparing it with the expression profile of the polynucleotide in a sample taken from the subject after treatment.

In accordance with the prognostic aspect of the invention, the treatment in conjunction  
25 with which the above methods of measuring the responsiveness of a subject to a cancer treatment may be employed include, for example, radiotherapy, surgical treatment, chemotherapy, and the like.

The methods disclosed herein may also be indicative of the status of a biomarker gene,  
30 as described above. Where a biomarker gene or a pathway in which such gene is involved is defective or abnormal, this information may also serve in prognosis of both disease progression and treatment responsiveness of a patient, regardless of whether said treatment is directed to the biomarker in question.

Methods for the identification of marker gene biomarkers for both diagnostic and therapeutic applications in any given cancer type. In certain embodiments, these methods use a combination of recently developed powerful functional gene cloning methodologies with cDNA array-based gene expression profiling and rationally designed experimental models.

- 5 Diagnostic and therapeutic value of the identified genes may then be evaluated using specific inhibitors and antibodies according to methods well known to those of skill in the art.

- By identifying those genes that are specifically upregulated (or indeed downregulated) in cancer cells as a result of biomarker regulation, the invention provides markers of advanced stages of cancer. More specifically, the invention relates to identifying potential biomarkers of biomarker regulation associated with early and advanced stages of the disease by performing micro-array hybridization and analyses using model cancer cell line(s) or primary normal cell cultures that retain wild-type biomarker activity and engineering a variant of such a cell line or primary cells in which the biomarker is inactivated. Alternatively, the tissue pairs for comparison will be normal animal tissues and the same cancer-free tissues from genetically modified animals in which a biomarker gene of interest was knocked out.
- 10
- 15

- The methods of the invention generally provide a systematic approach for the search of cancer markers or biomarkers for therapeutic intervention among the genes normally under control of biomarker proteins. These biomarker can be expressed discordantly or concordantly between RRR and RCC. If expressed concordantly it will reflect a gene expression which is conserved between cancer and wound healing and represent a therapeutic target which permits the tumor to respond to certain physiological signals that are known inhibit tissue regeneration. A discordantly expressed gene represent a divergent discordant (inverted) pattern of expression where gene expression changes are in opposite direction in RRR and RCC. Thus the discordant gene expression is marker for diagnostics and therapeutics of renal carcinoma or wound healing .
- 20
- 25

The methods of the invention may be performed by comparing gene expression profiles of the markers in cell lines or tissues.

An exemplary model for the screening methods of the invention is the ischemic/reperfusion injury model in rodents.

- 30 Selection of cancer or wound healing diagnostic markers, the following criteria were applied:

(1) genes that are concordantly expressed in RCC and RRR are useful as drug targets which permits the tumor or the wounded tissue to respond to certain physiological signals that are known inhibit or induce tissue regeneration,

(2) genes that are discordantly expressed in RCC and RRR are useful as diagnostic targets which distinct to these tumor or wound healing.

(3) genes that are discordantly expressed in RCC and RRR are useful as drug targets which permits the tumor or the wounded tissue to respond to certain physiological signals that are distinct to tumor or the wounded tissue, but not for both.

The genes identified in Table 1 – 13 are useful in diagnostic and prognostic application as well as act as drug biomarkers for therapeutic intervention of the diseased state.

#### **Diagnostic Methods of Using Identified Markers**

In the genetic diagnostic applications of the invention, one of skill in the art would detect variations, modulations, discordance, or concordance in the expression of one or more of the markers. This may comprise determining the mRNA level or expression patterns of the gene(s) or determining specific alterations in the expressed gene product(s). The cancers that may be diagnosed according to the invention include cancers of kidney or other tissue.

Discordant genes, as described herein and listed in Table 9, are expressed discordantly in RCC from RRR. The discordant signature can be used as a diagnostic and screening assays for kidney cancer and wound healing (i.e. acute renal failure and kidney transplantation).

Discordant gene expression analysis can also be used to diagnose ischemia, for example when shipping organs. The discordant signature or pattern of gene expression can be used to identify drugs and drugs combinations for use in anti cancer application and/or in slowing ischemia when shipping organs (i.e., if live donor, she/he will get the drug or the kidney will be treated with such drugs).

This method and data be useful for diagnosing and treatment of cancer or ischemia and wound healing in liver, lung, heart, esophagus, bone, intestine, breast, brain, uterine cervix, testis, stomach, prostate, or skin. Specifically in ischemia, acute renal failure renal, renal regeneration and repair, cyst, renal metastasis, renal cancers this method could be used in renal cell carcinoma, Wilms tumors (WT), Birt-Hogg-Dube' (BHD), and hereditary papillary renal-cell carcinoma (HPRC).

Nucleic acids can be isolated from cells contained in the biological sample, according to standard methodologies (Sambrook et al., 1989). The nucleic acid may be whole RNA, a mixture of RNA and DNA, mRNA, poly-A RNA, and the like. The nucleic acid sample, e.g.

RNA, may be used for Northern blotting analysis or may be converted to a complementary DNA (cDNA). cDNA may be used for preparation of probes for microarray hybridization or may be amplified in PCR reaction (RT-PCR).

Marker, (e.g., transcript) analysis may be by in situ hybridization using a labeled nucleic acid probe. The in situ hybridization is well known in the art.

Depending on the format, the specific nucleic acid of interest is identified in the sample directly using amplification or by hybridization to a labeled (radioactively or fluorescently) nucleic acid probe. The identified amplified product is then detected. In certain applications, the detection may be performed by visual means (e.g., ethidium bromide staining of a gel). Alternatively, the detection may involve indirect identification of the product via chemiluminescence, radioactive scintigraphy of radiolabel or fluorescent label or even via a system using electrical or thermal impulse signals (Affymax Technology; Bellus, 1994).

#### **Capture Of Markers**

Biomarkers are preferably captured with capture reagents immobilized to a solid support, such as any biochip described herein, a multiwell microtiter plate or a resin. The biomarkers of this invention may be captured on protein biochips or microarrays.

Microarrays useful in the methods of the invention for measuring tissue-specific gene expression comprise, for example, the biomarker or anti-sense biomarker polynucleotides, for example, a combination of biomarker and/or anti-sense biomarker polynucleotides from one or more trends. Alternately, the microarrays comprise at least 4 polynucleotides from Table 9 selected by their differential expression between cancerous and control samples. The invention further contemplates a method of diagnosing a cancer comprising contacting a cell sample nucleic acid with a microarray described herein under conditions suitable for hybridization; providing hybridization conditions suitable for hybrid formation between said cell sample nucleic acid and a polynucleotide of said microarray; detecting said hybridization; and diagnosing a cancer based on the results of detecting said hybridization.

Alternately, biomarkers may be captured on an antibody microarray. The antibody microarray comprises anti-biomarker antibodies, for example, a combination of anti-biomarker antibodies from one or more trends. Alternately, the microarrays comprise at least 4 antibodies that are anti-biomarker antibodies of gene products from Table 9 selected by their differential expression between cancerous and control cells. The invention further contemplates a method of diagnosing a cancer or wound healing comprising contacting a bodily fluid sample with the antibody microarray described herein, and detecting hybridization

between the antibodies present on the array and at least one polypeptide present in the bodily fluid, the results of said detection enabling a diagnosis or a prognosis of a cancer.

In general, a sample containing the biomarkers, such as a cell lysate, is placed on the active surface of a biochip for a sufficient time to allow binding. Then, unbound molecules are washed from the surface using a suitable eluant, such as phosphate buffered saline. In general, the more stringent the eluant, the more tightly the proteins must be bound to be retained after the wash. The retained protein biomarkers now can be detected by appropriate means.

#### DETECTION AND MEASUREMENT OF MARKERS

Once captured on a substrate, e.g., biochip or antibody, any suitable method can be used to measure a marker or markers in a sample. For example, markers can be detected and/or measured by a variety of detection methods including for example, gas phase ion spectrometry methods, optical methods, electrochemical methods, atomic force microscopy and radio frequency methods. Using these methods, one or more markers can be detected.

#### Microarray Analyses

The term "microarray" refers to an ordered arrangement of hybridizable array elements. The array elements are arranged so that there are preferably at least two or more different array elements, or for example at least 10, 15, 20, 25, 30, 35, 40, 45, 100, 1000, 2000, 3000, 4000 or more. Array elements are available commercially, for example, from Affymetrix, Inc. Array elements may be on, for example, a 1 cm<sup>2</sup> substrate surface. The hybridization signal from each of the array elements is individually distinguishable. In one embodiment, the array elements comprise polynucleotide probes. In another embodiment, the array elements comprise antibodies.

DNA-based arrays provide a convenient way to explore the expression of a single polymorphic gene or a large number of genes for a variety of applications. The one or more of the markers identified by the invention may be presented in a DNA microarray for the analysis and expression of these genes in various samples and controls. Microarray chips are well known to those of skill in the art (see, e.g., U.S. Pat. Nos. 6,308,170; 6,183,698; 6,306,643; 6,297,018; 6,287,850; 6,291,183, each incorporated herein by reference). These are exemplary patents that disclose nucleic acid microarrays and those of skill in the art are aware of numerous other methods and compositions for producing microarrays.

Protein and antibody microarrays are well known in the art (see, for example: Ekins R. P., J Pharm Biomed Anal 1989. 7: 155; Ekins R. P. and Chu F. W., Clin Chem 1991. 37: 1955;

Ekins R. P. and Chu F. W, Trends in Biotechnology, 1999, 17, 217-218). Antibody microarrays directed against a combination of the diagnostic markers disclosed herein will be very useful for the diagnosis of cancer markers in bodily fluids.

A plurality of polynucleotides identified according to the methods of the invention are useful as biomarkers for diagnosis, prognosis and screening assays described herein. . The polynucleotides may be about 9 nucleotides; alternately about 12, 15, 17, 20 nucleotides or longer, depending on the specific use. One of skill in the art would know what length polynucleotide would be appropriate for a particular purpose. Such a plurality of polynucleotides can be employed for the diagnosis and treatment of neoplastic disorder.

The plurality of polynucleotides and/or their anti-sense sequences are useful as hybridizable array elements in a microarray for monitoring the expression of a plurality of biomarker polynucleotides. The microarray comprises a substrate and the hybridizable array elements. The microarray is used, for example, in the diagnosis and treatment of a cancer.

In one aspect, the invention provides a microarray that is a low density array with 384 qPCR reactions to detect biomarkers of the invention in an RNA sample. Premade qPCR reactions for the human discordant genes and standard gene 18s were printed on a low density array (Applied Biosystems). The reactions were printed in replicas

#### IMMUNOASSAY

In another embodiment, an immunoassay can be used to detect and analyze markers in a sample. This method comprises: (a) providing an antibody that specifically binds to a marker; (b) contacting a sample with the antibody; and (c) detecting the presence of a complex of the antibody bound to the marker in the sample.

An immunoassay is an assay that uses an antibody to specifically bind an antigen (e.g., a marker). The immunoassay is characterized by the use of specific binding properties of a particular antibody to isolate, biomarker, and/or quantify the antigen. The phrase "specifically (or selectively) binds" to an antibody or "specifically (or selectively) immunoreactive with," when referring to a protein or peptide, refers to a binding reaction that is determinative of the presence of the protein in a heterogeneous population of proteins and other biologics. Thus, under designated immunoassay conditions, the specified antibodies bind to a particular protein at least two times the background and do not substantially bind in a significant amount to other proteins present in the sample. Specific binding to an antibody under such conditions may require an antibody that is selected for its specificity for a particular protein. For example, polyclonal antibodies raised to a marker from specific species such as rat, mouse, or human



can be selected to obtain only those polyclonal antibodies that are specifically immunoreactive with that marker and not with other proteins, except for polymorphic variants and alleles of the marker. This selection may be achieved by subtracting out antibodies that cross-react with the marker molecules from other species.

Using the purified markers or their nucleic acid sequences, antibodies that specifically bind to a marker can be prepared using any suitable methods known in the art. *See, e.g.,* Coligan, *Current Protocols in Immunology* (1991); Harlow & Lane, *Antibodies: A Laboratory Manual* (1988); Goding, *Monoclonal Antibodies: Principles and Practice* (2d ed. 1986); and Kohler & Milstein, *Nature* 256:495-497 (1975). Such techniques include, but are not limited to, antibody preparation by selection of antibodies from libraries of recombinant antibodies in phage or similar vectors, as well as preparation of polyclonal and monoclonal antibodies by immunizing rabbits or mice (*see, e.g.,* Huse *et al.*, *Science* 246:1275-1281 (1989); Ward *et al.*, *Nature* 341:544-546 (1989)). Typically a specific or selective reaction will be at least twice background signal or noise and more typically more than 10 to 100 times background.

Generally, a sample obtained from a subject can be contacted with the antibody that specifically binds the marker. Optionally, the antibody can be fixed to a solid support to facilitate washing and subsequent isolation of the complex, prior to contacting the antibody with a sample. Examples of solid supports include glass or plastic in the form of, *e.g.,* a microtiter plate, a stick, a bead, or a microbead. Antibodies can also be attached to a probe substrate or ProteinChip<sup>®</sup> array described above. The sample is preferably a biological fluid sample taken from a subject. Examples of biological fluid samples include blood, serum, plasma, nipple aspirate, urine, tears, saliva *etc.* In a preferred embodiment, the biological fluid comprises blood serum. The sample can be diluted with a suitable eluant before contacting the sample to the antibody.

After incubating the sample with antibodies, the mixture is washed and the antibody-marker complex formed can be detected. This can be accomplished by incubating the washed mixture with a detection reagent. This detection reagent may be, *e.g.,* a second antibody which is labeled with a detectable label. Exemplary detectable labels include magnetic beads (*e.g.,* DYNABEADS<sup>TM</sup>), fluorescent dyes, radiolabels, enzymes (*e.g.,* horse radish peroxidase, alkaline phosphatase and others commonly used in an ELISA), and colorimetric labels such as colloidal gold or colored glass or plastic beads. Alternatively, the marker in the sample can be detected using an indirect assay, wherein, for example, a second, labeled antibody is used to detect bound marker-specific antibody, and/or in a competition or inhibition assay wherein, for

example, a monoclonal antibody which binds to a distinct epitope of the marker is incubated simultaneously with the mixture.

Methods for measuring the amount of, or presence of, antibody-marker complex include, for example, detection of fluorescence, luminescence, chemiluminescence, absorbance, reflectance, transmittance, birefringence or refractive index (e.g., surface plasmon resonance, ellipsometry, a resonant mirror method, a grating coupler waveguide method or interferometry). Optical methods include microscopy (both confocal and non-confocal), imaging methods and non-imaging methods. Electrochemical methods include voltammetry and amperometry methods. Radio frequency methods include multipolar resonance spectroscopy. Methods for performing these assays are readily known in the art. Useful assays include, for example, an enzyme immune assay (EIA) such as enzyme-linked immunosorbent assay (ELISA), a radioimmune assay (RIA), a Western blot assay, or a slot blot assay. These methods are also described in, e.g., *Methods in Cell Biology: Antibodies in Cell Biology*, volume 37 (Asai, ed. 1993); *Basic and Clinical Immunology* (Stites & Terr, eds., 7th ed. 1991); and Harlow & Lane, *supra*.

Throughout the assays, incubation and/or washing steps may be required after each combination of reagents. Incubation steps can vary from about 5 seconds to several hours, preferably from about 5 minutes to about 24 hours. However, the incubation time will depend upon the assay format, marker, volume of solution, concentrations and the like. Usually the assays will be carried out at ambient temperature, although they can be conducted over a range of temperatures, such as 10°C to 40°C.

Immunoassays can be used to determine presence or absence of a marker in a sample as well as the quantity of a marker in a sample. The amount of an antibody-marker complex can be determined by comparing to a standard. A standard can be, e.g., a known compound or another protein known to be present in a sample. As noted above, the test amount of marker need not be measured in absolute units, as long as the unit of measurement can be compared to a control.

The methods for detecting these markers in a sample have many applications. For example, one or more markers can be measured to aid human cancer diagnosis or prognosis. In another example, the methods for detection of the markers can be used to monitor responses in a subject to cancer treatment. In another example, the methods for detecting markers can be used to assay for and to identify compounds that modulate expression of these markers *in vivo* or *in vitro*. In a preferred example, the biomarkers are used to differentiate between the

different stages of tumor progression, thus aiding in determining appropriate treatment and extent of metastasis of the tumor.

The term "probe" refers to a polynucleotide sequence capable of hybridizing with a biomarker sequence to form a polynucleotide probe/biomarker complex. A "biomarker polynucleotide" refers to a chain of nucleotides to which a polynucleotide probe can hybridize by base pairing. In some instances, the sequences will be complementary (no mismatches) when aligned. In other instances, there may be up to a 10% mismatch. Alternatively, the term "probe" may refer to a polypeptide probe that can hybridize to an antibody.

A "plurality" refers preferably to a group of at least 3 or more members, more preferably to a group of at least about 10, 50, 100, and at least about 1,000, members. The maximum number of members is unlimited, but is at least about 100,000 members.

The term "gene" or "genes" refers to a polynucleotide sequence(s) of a gene, which may be the partial or complete sequence of the gene and may comprise regulatory region(s), untranslated region(s), or coding regions.

The polynucleotide or antibody microarray can be used for large-scale genetic or gene expression analysis of a large number of biomarker polynucleotides or polypeptides respectively. The microarray can also be used in the diagnosis of diseases and in the monitoring of treatments. Further, the microarray can be employed to investigate an individual's predisposition to a disease. Furthermore, the microarray can be employed to investigate cellular responses to infection, drug treatment, and the like.

When the composition of the invention is employed as hybridizable array elements in a microarray, the array elements are organized in an ordered fashion so that each element is present at a distinguishable, and preferably specified, location on the substrate. In the preferred embodiments, because the array elements are at specified locations on the substrate, the hybridization patterns and intensities (which together create a unique expression profile) can be interpreted in terms of expression pattern of particular genes and can be correlated with a particular disease or condition or treatment.

The composition comprising a plurality of polynucleotide probes can also be used to purify a subpopulation of mRNAs, cDNAs, genomic fragments and the like, in a sample. Typically, samples will include biomarker polynucleotides of interest and other nucleic acids which may enhance the hybridization background; therefore, it may be advantageous to remove these nucleic acids from the sample. One method for removing the additional nucleic acids is by hybridizing the sample containing biomarker polynucleotides with immobilized

polynucleotide probes under hybridizing conditions. Those nucleic acids that do not hybridize to the polynucleotide probes are removed and may be subjected to analysis or discarded. At a later point, the immobilized biomarker polynucleotide probes can be released in the form of purified biomarker polynucleotides.

## 5 **Microarrays**

### **Microarray Expression Profiles - Expression Profiling**

An expression profile can be used to detect changes in the expression of genes implicated in disease. Changes in expression include, up and/or down regulation of a gene.

The expression profile includes a plurality of detectable complexes. Each complex is  
10 formed by hybridization of one or more, polynucleotides of the invention to one or more complementary biomarker polynucleotides. At least one of the polynucleotides of the invention, and preferably a plurality thereof, is hybridized to a complementary biomarker polynucleotide forming at least one, and preferably a plurality, of complexes. A complex is detected by incorporating at least one labeling moiety in the complex as described above. The  
15 expression profiles provide "snapshots" that can show unique expression patterns that are characteristic of the presence or absence of a disease or condition.

After performing hybridization experiments and interpreting detected signals from a microarray, particular probes can be identified and selected based on their expression patterns. Such probe sequences can be used to clone a full-length sequence for the gene or to produce a  
20 polypeptide.

The composition comprising a plurality of probes can be used as hybridizable elements in a microarray. Such a microarray can be employed in several applications including diagnostics, prognostics and treatment regimens, drug discovery and development, toxicological and carcinogenicity studies, forensics, pharmacogenomics, and the like.

25 The invention provides for microarrays for measuring gene expression characteristic of a cancer of a tissue, comprising at least 4 polypeptide encoding polynucleotides or at least 4 antibodies which bind specifically to the polypeptides encoded by these polynucleotides, as listed in Table 2 and according to the following:

A microarray for measuring gene expression characteristic of renal cancer comprising  
30 markers listed in Table 2 sheet 1; A microarray for measuring gene expression characteristic of uterine cancer comprising markers listed in Table 2 sheet 2; A microarray for measuring gene expression characteristic of kidney cancer comprising markers listed in Table 2 sheet 3; A microarray for measuring gene expression characteristic of bladder cancer comprising

markers listed in Table 2 sheet 4; A microarray for measuring gene expression characteristic of lung cancer comprising markers listed in Table 2 sheet 5; A microarray for measuring gene expression characteristic of brain cancer comprising markers listed in Table 2 sheet 6; A microarray for measuring gene expression characteristic of colon cancer comprising markers listed in Table 2 sheet 7; A microarray for measuring gene expression characteristic of intestinal cancer comprising markers listed in Table 2 sheet 8; A microarray for measuring gene expression characteristic of stomach cancer comprising markers listed in Table 2, sheet 9; A microarray for measuring gene expression characteristic of renal cancer comprising markers listed in Table 2 sheet 10; A microarray for measuring gene expression characteristic of pancreatic cancer comprising markers listed in Table 2 sheet 11; and A microarray for measuring gene expression characteristic of spleen cancer comprising markers listed in Table 2 sheet 12.

The nucleic acid probes can be genomic DNA or cDNA or mRNA, or any RNA-like or DNA-like material, such as peptide nucleic acids, branched DNAs, and the like. The probes can be sense or antisense polynucleotide probes. Where biomarker polynucleotides are double-stranded, the probes may be either sense or antisense strands. Where the biomarker polynucleotides are single-stranded, the probes are complementary single strands.

In one embodiment, the probes are cDNAs. The size of the DNA sequence of interest may vary and is preferably from 100 to 10,000 nucleotides, more preferably from 150 to 3,500 nucleotides. The probes can be prepared by a variety of synthetic or enzymatic schemes, which are well known in the art. The probes can be synthesized, in whole or in part, using chemical methods well known in the art (Caruthers et al., *Nucleic Acids Res.*, Symp. Ser., 215-233 (1980). Alternatively, the probes can be generated, in whole or in part, enzymatically. Nucleotide analogs can be incorporated into the probes by methods well known in the art. The only requirement is that the incorporated nucleotide analog must serve to base pair with biomarker polynucleotide sequences. For example, certain guanine nucleotides can be substituted with hypoxanthine, which base pairs with cytosine residues. However, these base pairs are less stable than those between guanine and cytosine. Alternatively, adenine nucleotides can be substituted with 2,6-diaminopurine, which can form stronger base pairs than those between adenine and thymidine. Additionally, the probes can include nucleotides that have been derivatized chemically or enzymatically. Typical chemical modifications include derivatization with acyl, alkyl, aryl or amino groups. The polynucleotide probes can be immobilized on a substrate. Preferred substrates are any suitable rigid or semi-rigid support including membranes, filters, chips, slides, wafers, fibers, magnetic or nonmagnetic

beads, gels, tubing, plates, polymers, microparticles and capillaries. The substrate can have a variety of surface forms, such as wells, trenches, pins, channels and pores, to which the polynucleotide probes are bound. Preferably, the substrates are optically transparent.

Complementary DNA (cDNA) can be arranged and then immobilized on a substrate. The

- 5 probes can be immobilized by covalent means such as by chemical bonding procedures or UV. In one such method, a cDNA is bound to a glass surface which has been modified to contain epoxide or aldehyde groups. In another case, a cDNA probe is placed on a polylysine coated surface and then UV cross-linked (Shalon et al., PCT publication WO95/35505, herein incorporated by reference). In yet another method, a DNA is actively transported from a
- 0 solution to a given position on a substrate by electrical means (Heller et al., U.S. Pat. No. 5,605,662). Alternatively, individual DNA clones can be gridded on a filter. Cells are lysed, proteins and cellular components degraded, and the DNA coupled to the filter by UV cross-linking.

- Furthermore, the probes do not have to be directly bound to the substrate, but rather
- 5 can be bound to the substrate through a linker group. The linker groups are typically about 6 to 50 atoms long to provide exposure to the attached probe. Preferred linker groups include ethylene glycol oligomers, diamines, diacids and the like. Reactive groups on the substrate surface react with one of the terminal portions of the linker to bind the linker to the substrate. The other terminal portion of the linker is then functionalized for binding the probe.

- 20 The probes can be attached to a substrate by dispensing reagents for probe synthesis on the substrate surface or by dispensing preformed DNA fragments or clones on the substrate surface. Typical dispensers include a micropipette delivering solution to the substrate with a robotic system to control the position of the micropipette with respect to the substrate. There can be a multiplicity of dispensers so that reagents can be delivered to the reaction regions
- 25 simultaneously.

- Alternatively, as mentioned above, antibody microarrays can be produced. The production of such microarrays is essentially as described in Schweitzer & Kingsmore, "Measuring proteins on microarrays", *Curr Opin Biotechnol* 2002; 13(1): 14-9; Avseenko et al., "Immobilization of proteins in immunochemical microarrays fabricated by electrospray
- 30 deposition", *Anal Chem* 2001 15; 73(24): 6047-52; Huang, "Detection of multiple proteins in an antibody-based protein microarray system, *Immunol Methods* 2001 1; 255 (1-2): 1-13. In general, protein microarrays may be produced essentially as described in Schemm et al., *Parallel human genome analysis: Microarray-based expression monitoring of 1000 genes. Proc. Natl. Sci. USA* (1996) 93, 10614-10619; U.S. Pat. Nos. 6,291,170 and 5,807,522 (see above); U.S.

Pat. No. 6,037,186 (Stimpson, inventor) "Parallel production of high density arrays"; PCT publications WO 99/13313 (Genovations Inc (US), applicant) "Method of making high density arrays"; WO 02/05945 (Max-Delbruck-center for molecular medicine (Germany), applicant) "Method for producing microarray chips with nucleic acids, proteins or other test substrates".

### Hybridization and Detection in Microarrays

Hybridization causes a denatured probe and a denatured complementary biomarker to form a stable nucleic acid duplex through base pairing. Hybridization methods are well known to those skilled in the art (See, e.g., Ausubel, Short Protocols in Molecular Biology, John Wiley & Sons, New York N.Y., units 2.8-2.11, 3.18-3.19 and 4-6-4.9, 1997). Conditions can be selected for hybridization where an exactly complementary biomarker and probes can hybridize, i.e., each base pair must interact with its complementary base pair. Alternatively, conditions can be selected where a biomarker and probes have mismatches but are still able to hybridize. Suitable conditions can be selected, for example, by varying the concentrations of salt in the prehybridization, hybridization and wash solutions, by varying the hybridization and wash temperatures, or by varying the polarity of the prehybridization, hybridization or wash solutions.

Hybridization can be performed at low stringency with buffers, such as 6XSSPE with 0.005% Triton X-100 at 37°C., which permits hybridization between biomarker and probes that contain some mismatches to form biomarker polynucleotide/probe complexes. Subsequent washes are performed at higher stringency with buffers, such as 0.5XSSPE with 0.005% Triton X-100 at 50°C, to retain hybridization of only those biomarker/probe complexes that contain exactly complementary sequences. Alternatively, hybridization can be performed with buffers, such as 5XSSC/0.2% SDS at 60°C. and washes are performed in 2XSSC/0.2% SDS and then in 0.1XSSC. Background signals can be reduced by the use of detergent, such as sodium dodecyl sulfate, Sarcosyl or Triton X-100, or a blocking agent, such as salmon sperm DNA.

After hybridization, the microarray is washed to remove nonhybridized nucleic acids, and complex formation between the hybridizable array elements and the biomarker polynucleotides is detected. Methods for detecting complex formation are well known to those skilled in the art. In a preferred embodiment, the biomarker polynucleotides are labeled with a fluorescent label, and measurement of levels and patterns of fluorescence indicative of complex formation is accomplished by fluorescence microscopy, preferably confocal fluorescence microscopy. An argon ion laser excites the fluorescent label, emissions are directed to a photomultiplier, and the amount of emitted light is detected and quantitated. The

detected signal should be proportional to the amount of probe/biomarker polynucleotide complex at each position of the microarray. The fluorescence microscope can be associated with a computer-driven scanner device to generate a quantitative two-dimensional image of hybridization intensity. The scanned image is examined to determine the \*

5 abundance/expression level of each hybridized biomarker polynucleotide.

Typically, microarray fluorescence intensities can be normalized to take into account variations in hybridization intensities when more than one microarray is used under similar test conditions. In a preferred embodiment, individual probe/biomarker hybridization intensities are normalized using the intensities derived from internal normalization controls  
10 contained on each microarray.

Protein or antibody microarray hybridization is carried out essentially as described in Ekins et al. *J Pharm Biomed Anal* 1989, 7: 155; Ekins and Chu, *Clin Chem* 1991, 37: 1955; Ekins and Chu, *Trends in Biotechnology*, 1999, 17, 217-218; MacBeath and Schreiber, *Science* 2000; 289(5485): p. 1760-1763.

#### 15 **Sample Preparation for Genetic Analysis**

To conduct sample analysis, a sample containing biomarker polynucleotides or polypeptides is provided. The samples can be any sample containing biomarker polynucleotides or polypeptides and obtained from any bodily fluid (blood, sperm, urine, saliva, phlegm, gastric juices, etc. as described herein), cultured cells, biopsies, or other tissue  
20 preparations. The samples being analyzed using the microarrays will likely be samples from individuals suspected of suffering from a given cancer. In one embodiment, the microarrays used are those that contain tumor markers specific for that cancer or antibodies against those markers.

DNA or RNA can be isolated from the sample according to any of a number of  
25 methods well known to those of skill in the art. For example, methods of purification of nucleic acids are described in Tijssen *Laboratory Techniques in Biochemistry and Molecular Biology: Hybridization With Nucleic Acid Probes, Part I. Theory and Nucleic Acid Preparation*, Elsevier, New York N.Y. 1993. In one case, total RNA is isolated using the TRIZOL reagent (Life Technologies, Gaithersburg Md.), and mRNA is isolated using oligo  
30 d(T) column chromatography or glass beads. Alternatively, when biomarker polynucleotides are derived from an mRNA, the biomarker polynucleotides can be a cDNA reverse-transcribed from an mRNA, an RNA transcribed from that cDNA, a DNA amplified from that cDNA, an RNA transcribed from the amplified DNA, and the like. When the biomarker polynucleotide is



derived from DNA, the biomarker polynucleotide can be DNA amplified from DNA or RNA reverse transcribed from DNA. In yet another alternative, the biomarkers are biomarker polynucleotides prepared by more than one method.

When biomarker polynucleotides are amplified, it is desirable to amplify the nucleic acid sample and maintain the relative abundances of the original sample, including low abundance transcripts. Total mRNA can be amplified by reverse transcription using a reverse transcriptase and a primer consisting of oligo d(T) and a sequence encoding the phage T7 promoter to provide a single-stranded DNA template. The second DNA strand is polymerized using a DNA polymerase and a RNase which assists in breaking up the DNA/RNA hybrid. After synthesis of the double-stranded DNA, T7 RNA polymerase can be added, and RNA transcribed from the second DNA strand template (Van Gelder et al. U.S. Pat. No. 5,545,522). RNA can be amplified in vitro, in situ or in vivo (See Eberwine, U.S. Pat. No. 5,514,545).

Controls may be included within the sample to assure that amplification and labeling procedures do not change the true distribution of biomarker polynucleotides in a sample. For this purpose, a sample is spiked with a known amount, of a control biomarker polynucleotide and the composition of probes includes reference probes which specifically hybridize with the control biomarker polynucleotides. After hybridization and processing, the hybridization signals obtained should accurately the amounts of control biomarker polynucleotide added to the sample.

Prior to hybridization, it may be desirable to fragment the nucleic acid biomarker polynucleotides. Fragmentation improves hybridization by minimizing secondary structure and cross-hybridization to other nucleic acid biomarker polynucleotides in the sample or noncomplementary polynucleotide probes. Fragmentation can be performed by mechanical or chemical means.

Antibodies against the relevant cancer marker polypeptides and appropriate for attachment to an antibody microarray can be prepared according to methods known in the art (Coligan et al, Unit 9, Current Protocols in Immunology, Wiley Interscience, 1994; Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, New York (1988). Additional information regarding all types of antibodies, including humanized antibodies, human antibodies and antibody fragments can be found in WO 01/05998).

Polypeptides can be prepared for hybridization to an antibody microarray from a sample, such as a bodily fluid sample, according to methods known in the art. It may be desirable to purify the proteins from the sample or alternatively, to remove certain impurities

which may be present in the sample and interfere with hybridization. Protein purification is practiced as is known in the art as described in, for example, Marshak et al., "Strategies for Protein Purification and Characterization. A laboratory course manual." CSHL Press (1996).

The biomarker polynucleotides or polypeptides may be labeled with one or more labeling moieties to allow for detection of hybridized probe/biomarker complexes. The labeling moieties can include compositions that can be detected by spectroscopic, photochemical, biochemical, bioelectronic, immunochemical, electrical, optical or chemical means. The labeling moieties include radioisotopes, such as  $^3\text{H}$ ,  $^{14}\text{C}$ ,  $^{32}\text{P}$ ,  $^{33}\text{P}$  or  $^{35}\text{S}$ , chemiluminescent compounds, labeled binding proteins, heavy metal atoms, spectroscopic markers, such as fluorescent markers and dyes, magnetic labels, linked enzymes, mass spectrometry tags, spin labels, electron transfer donors and acceptors, and the like.

Exemplary dyes include quinoline dyes, triarylmethane dyes, phthaleins, azo dyes, cyanine dyes, and the like. Preferably, fluorescent markers absorb light above about 300 nm, preferably above 400 nm, and usually emit light at wavelengths at least greater than 10 nm above the wavelength of the light absorbed. Preferred fluorescent markers include fluorescein, phycoerythrin, rhodamine, lissamine, and C3 and C5 available from Amersham Pharmacia Biotech (Piscataway N.J.).

Nucleic acid labeling can be carried out during an amplification reaction, such as polymerase chain reactions and in vitro transcription reactions, or by nick translation or 5' or 3'-end-labeling reactions. When the label may be incorporated after or without an amplification step, the label is incorporated by using terminal transferase or by phosphorylating the 5' end of the biomarker polynucleotide using, e.g., a kinase and then incubating overnight with a labeled oligonucleotide in the presence of T4 RNA ligase. Alternatively, the labeling moiety can be incorporated after hybridization once a probe/biomarker complex has formed.

Polypeptide labeling can be conducted using a variety of techniques well known in the art, and the choice of the technique(s) can be tailored to the polypeptide in question according to criteria known to one of skill in the art. Specifically, polypeptides can be fluorescently labeled with compounds such as FITC or rhodamin, essentially as described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, New York (1988), in particular pages 353-356, or with other fluorescent compounds such as nile red or 2-methoxy-2,4-diphenyl-3(2H)furanone (Daban: *Electrophoresis* 2001; 22(5): 874-80). Polypeptides can also be labeled with a detectable protein such as GFP (detection based on

fluorescence) or the vitamin biotin (detection with streptavidin). Polypeptides can also be radioactively labeled with the isotope  $S^{35}$ . Additional methods are widely known in the art.

#### Use of Gene Sequences for Diagnostic Purposes

In certain embodiments, the tissue-specific tumor markers identified herein may be used for the diagnosis of advanced stages of cancer in the given tissue for which the markers are specific. The polynucleotide sequences encoding the tissue specific tumor marker or the polypeptide encoded thereby, where appropriate, may be used in in-situ hybridization or RT-PCR assays of fluids or tissues from biopsies to detect abnormal gene expression. Such methods may be qualitative or quantitative in nature and may include Southern or Northern analysis, dot blot or other membrane-based technologies; PCR technologies; chip based technologies (for nucleic acid detection) and dip stick, pin, ELISA and protein-chip technologies (for the detection of polypeptides). All of these techniques are well known in the art and are the basis of many commercially available diagnostic kits.

In addition, such assays may be useful in evaluating the efficacy of a particular therapeutic treatment regime in animal studies, in clinical trials, or in monitoring the treatment of an individual patient. Such monitoring may generally employ a combination of body fluids or cell extracts taken from normal subjects, either animal or human, under conditions suitable for hybridization or amplification. Standard hybridization may be quantified by comparing the values obtained for normal subjects with a dilution series of a tissue-specific tumor marker gene product run in the same experiment where a known amount of purified gene product is used. Standard values obtained from normal samples may be compared with values obtained from samples from cachectic subjects affected by abnormal gene expression in tumor cells. Deviation between standard and subject values establishes the presence of disease.

Generally, the tissue-specific tumor markers are chosen based on the specificity of their expression in tumors as well as on the high correlation of the reactivity of corresponding antibodies with tumor specimens in ELISA and tissue arrays may be used for development of serological screening procedure. For example, in the context of prostate-specific tumor markers, a large scale analysis of serum and sperm samples obtained from normal donors of different age (before and after 60), patients with different grades and types of prostate carcinoma, androgen dependent and androgen independent, with local, recurrent and metastatic disease, patients with tumors of other than prostate origin, as well as patients with noncancerous diseases of prostate may be tested by ELISA on the presence and concentration of the potential candidate polypeptide(s). Then statistical analyses may be performed to evaluate whether the prostate samples express candidate(s) at different expression patterns

based on different parameters (histopathological type, Gleason score, tumor size, disease or PSA recurrence).

Once disease is established, a therapeutic agent is administered; and a treatment profile is generated. Such assays may be repeated on a regular basis to evaluate whether the values in the profile progress toward or return to the normal or standard pattern. Successive treatment profiles may be used to show the efficacy of treatment over a period of several days or several-months.

Polymerase Chain Reaction (PCR) as described in, for example, U.S. Pat. Nos. 4,683,195 and 4,965,188, provides additional uses for oligonucleotides specific for the tissue-specific tumor marker genes. Such oligomers are generally chemically synthesized, but they may be generated enzymatically or produced from a recombinant source as described herein above. Oligomers generally comprise two nucleotide sequences, one with sense orientation and one with antisense orientation, employed under optimized conditions for identification of a specific gene or condition. The same two oligomers, nested sets of oligomers, or even a degenerate pool of oligomers may be employed under less stringent conditions for detection and/or quantitation of closely related DNA or RNA sequences. Methods of performing RT-PCR are standard in the art and the method may be carried out using commercially available kits. Other PCR techniques are well known to one of skill in the art, and include, for example, qPCR, real time PCR, reverse transcriptase PCR, PCR done in high density arrays, e.g., open arrays.

Additionally, methods to quantitate the expression of a particular molecule include radiolabeling (Melby et al., J Immunol Methods, 159: 235-244 (1993) or biotinylating (Duplaa et al., Anal Biochem, 229: 226 (1993) nucleotides, coamplification of a control nucleic acid, and standard curves onto which the experimental results are interpolated. Quantitation of multiple samples may be speeded up by running the assay in an ELISA-like format where the oligomer of interest is presented in various dilutions and a spectrophotometric or colorimetric response gives rapid quantitation. For example, the presence of abnormal levels or expression patterns of a tissue-specific tumor marker in extracts of biopsied tissues will be indicative of the onset of a cancer. A definitive diagnosis of this type may allow health professionals to begin aggressive treatment and prevent further worsening of the condition. Similarly, further assays can be used to monitor the progress of a patient during treatment.

### **Immunodiagnosis and Polypeptide Detection**

In certain embodiments, antibodies may be used in characterizing the tissue-specific tumor marker content of healthy and diseased tissues, through techniques such as ELISAs, immunohistochemical detection and Western blotting.

This may provide a screen for the presence or absence of malignancy or as a predictor of future cancer. Once the tissue-specific tumor marker is identified, one of skill in the art may produce antibodies against that marker using techniques well known to those of skill in the art

The use of such antibodies in an ELISA assay is contemplated. For example,; such antibodies are immobilized onto a selected surface, preferably a surface exhibiting a protein affinity such as the wells of a polystyrene microtiter plate. After washing to remove incompletely adsorbed material, it is desirable to bind or coat the assay plate wells with a non-specific protein that is known to be antigenically neutral with regard to the test antisera such as bovine serum albumin (BSA), casein or solutions of powdered milk. This allows for blocking of non-specific adsorption sites on the immobilizing surface and thus reduces the background caused by non-specific binding of antigen onto the surface.

After binding of antibody to the well, coating with a non-reactive material to reduce background, and washing to remove unbound material, the immobilizing surface is contacted with the biological sample to be tested in a manner conducive to immune complex (antigen/antibody) formation.

Following formation of specific immunocomplexes between the test sample and the bound antibody, and subsequent washing, the occurrence and even amount of immunocomplex formation may be determined by subjecting same to a second antibody having specificity for the tumor marker that differs from the first antibody. Appropriate conditions preferably include diluting the sample with diluents such as BSA, bovine gamma globulin (BGG) and phosphate buffered saline (PBS)/Tween. These added agents also tend to assist in the reduction of nonspecific background. The layered antisera is then allowed to incubate for from about 2 to about 4 hr, at temperatures preferably on the order of about 25°C. to about 27°C. Following incubation, the antisera-contacted surface is washed so as to remove non-immunocomplexed material. A preferred washing procedure includes washing with a solution such as PBS/Tween, or borate buffer.

For convenient detection purposes, the second antibody may preferably have an associated enzyme that will generate a color development upon incubating with an appropriate chromogenic substrate. Thus, for example, one will desire to contact and incubate the second antibody-bound surface with a urease or peroxidase-conjugated anti-human IgG for a period of

time and under conditions which favor the development of immunocomplex formation (e.g., incubation for 2 hr at room temperature in a PBS-containing solution such as PBS/Tween).

After incubation with the second enzyme-tagged antibody, and subsequent to washing to remove unbound material, the amount of label is quantified by incubation with a chromogenic substrate such as urea and bromocresol purple or 2,2'-azino-di-(3-ethylbenzthiazoline)-6-sulfonic acid (ABTS) and hydrogen peroxide, in the case of peroxidase as the enzyme- label. Quantitation is then achieved by measuring the degree of color generation, e.g., using a visible spectrum spectrophotometer.

The preceding format may be altered by first binding the sample to the assay plate. Then, primary antibody is incubated with the assay plate, followed by detecting of bound primary antibody using a labeled second antibody with specificity for the primary antibody.

Immunoblotting and immunohistochemical techniques using antibodies directed against the tumor markers also are contemplated by the invention. The antibodies may be used as high-affinity primary reagents for the identification of proteins immobilized onto a solid support matrix, such as nitrocellulose, nylon or combinations thereof. In conjunction with immunoprecipitation, followed by gel electrophoresis, these may be used as a single step reagent for use in detecting antigens against which secondary reagents used in the detection of the antigen cause an adverse background. Immunologically-based detection methods for use in conjunction with Western blotting include enzymatically-, radiolabel-, or fluorescently-tagged secondary antibodies against the toxin moiety are considered to be of particular use in this regard.

Flow cytometry methods also may be used in conjunction with the invention. Methods of performing flow cytometry are discussed in Zhang et al., J Immunology, 157:3980-3987 (1996) and Pepper et al., Leuk. Res., 22(5):439-444 (1998). Generally, the cells, preferably blood cells, are permeabilized to allow the antibody to enter and exit the cell. If the gene in question encodes a cell surface protein, the step of permeabilization is not needed. After permeabilization, the cells are incubated with an antibody. In preferred embodiments, the antibody is a monoclonal antibody. It is more preferred that the monoclonal antibody be labeled with a fluorescent marker. If the antibody is not labeled with a fluorescent marker, a second antibody that is immunoreactive with the first antibody and contains a fluorescent marker. After sufficient washing to ensure that excess or non-bound antibodies are removed, the cells are ready for flow cytometry. If the marker is an enzyme, the reaction monitoring its specific enzymatic activity either in situ or in body fluids may be performed.

Determining the expression pattern of a polypeptide in a sample for the purposes of diagnosis may also be carried out in the form of enzymatic activity testing, when the polypeptide being examined offers such an option.

In addition, whole body image analysis following injection of labeled antibodies against cell surface marker proteins is a diagnostic possibility, as described above; the detected concentrations of such antibodies are indicative of the sites of tumor/ metastases growth as well as their number and the tumor size.

#### **Therapeutic Methods of Using Identified Markers**

The genes identified by the invention herein as down-regulated by the loss of a biomarker may prove effective against a given cancer when delivered therapeutically to the cancer cells. Antisense constructs of the genes identified herein as up-regulated as a result of loss of biomarker can be delivered therapeutically to cancer cells. Other therapeutic possibilities include siRNA, RNAi or small molecules or antibodies inhibiting the biomarker protein function and/or expression. The goal of such therapy is to retard the growth rate of the cancer cells. Expression of the sense molecules and their translation products or expression of the antisense mRNA molecules has the effect of inhibiting the growth rate of cancer cells or inducing apoptosis. Sense nucleic acid molecules are preferably delivered in constructs wherein a promoter is operatively linked to the coding sequence at the 5'-end and initiates transcription of the coding sequence. Anti-sense constructs contain a promoter operatively linked to the coding sequence at the 3'-end such that upon initiation of transcription at the promoter an RNA molecule is transcribed which is the complementary strand from the native mRNA molecule of the gene.

Delivery of nucleic acid molecules can be accomplished by many means known in the art. Gene delivery vehicles are available for delivery of polynucleotides to cells, tissue, or to a mammal for expression.

#### **Antibodies**

In one aspect, antibodies can be produced that are specific to one or more of the biomarkers listed in Table 9. The antibodies may be used, for example, to detect the biomarkers in the screening and diagnostic methods according to the invention. The antibodies may also be made into an antibody array for use in the methods of the invention.

Various procedures known in the art may be used for the production of antibodies against the biomarkers, or fragments, derivatives, homologs or analogs of the proteins. Antibodies of the invention include, but are not limited to, synthetic antibodies, monoclonal

antibodies, recombinantly produced antibodies, intrabodies, multispecific antibodies (including bi-specific antibodies), human antibodies, humanized antibodies, chimeric antibodies, synthetic antibodies, single-chain Fvs (scFv) (including bi-specific scFvs), single chain antibodies Fab fragments, F(ab') fragments, disulfide-linked Fvs (sdFv), and anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments of any of the above. In particular, antibodies of the present invention include immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site that immunospecifically binds to an antigen (*e.g.*, one or more complementarity determining regions (CDRs) of an antibody).

For production of the antibody, various host animals can be immunized by injection with, *e.g.*, a native biomarker protein or a synthetic version, or a derivative of the foregoing. Such host animals include, but are not limited to, rabbits, mice, rats, etc. Various adjuvants can be used to increase the immunological response, depending on the host species, and include, but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, and potentially useful human adjuvants such as bacille Calmette-Guerin (BCG) and *Corynebacterium parvum*. Although the following refers specifically to a biomarker, any of the methods described herein apply equally to a biomarker, concordantly or discordantly expressed gene family members or subunits thereof.

For preparation of monoclonal antibodies directed towards a biomarker, any technique that provides for the production of antibody molecules by continuous cell lines in culture may be used. Such techniques include, but are not restricted to, the hybridoma technique originally developed by Kohler and Milstein (1975, *Nature* 256:495-497), the trioma technique (Gustafsson *et al.*, 1991, *Hum. Antibodies Hybridomas* 2:26-32), the human B-cell hybridoma technique (Kozbor *et al.*, 1983, *Immunology Today* 4:72), and the EBV hybridoma technique to produce human monoclonal antibodies (Cole *et al.*, 1985, In: *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96). In an additional embodiment of the invention, monoclonal antibodies can be produced in germ-free animals utilizing recent technology described in International Patent Application PCT/US90/02545.

According to the present invention, human antibodies may be used and can be obtained by using human hybridomas (Cote *et al.*, 1983, *Proc. Natl. Acad. Sci. USA* 80:2026-2030) or by transforming human B cells with EBV virus in vitro (Cole *et al.*, 1985, In: *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96). In fact, according



to the invention, techniques developed for the production of "chimeric antibodies" (Morrison *et al.*, 1984, Proc. Natl. Acad. Sci. USA 81:6851-6855; Neuberger *et al.*, 1984, Nature 312:604-608; Takeda *et al.*, 1985, Nature 314:452-454) by splicing the genes from a mouse antibody molecule specific for a biomarker together with genes from a human antibody molecule of appropriate biological activity can be used; such antibodies are within the scope of this invention.

According to the present invention, techniques described for the production of single chain antibodies (U.S. Patent 4,946,778) can be adapted to produce a biomarker -specific antibodies. An additional embodiment of the invention utilizes the techniques described for the construction of Fab expression libraries (Huse *et al.*, 1989, Science 246:1275-1281) to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity for a biomarker proteins. Non-human antibodies can be "humanized" by known methods (*e.g.*, U.S. Patent No. 5,225,539).

Antibody fragments that contain the idiotypes of a biomarker can be generated by techniques known in the art. For example, such fragments include, but are not limited to, the F(ab')<sub>2</sub> fragment which can be produced by pepsin digestion of the antibody molecule; the Fab' fragment that can be generated by reducing the disulfide bridges of the F(ab')<sub>2</sub> fragment; the Fab fragment that can be generated by treating the antibody molecular with papain and a reducing agent; and Fv fragments. Synthetic antibodies, *e.g.*, antibodies produced by chemical synthesis, are useful in the present invention.

In the production of antibodies, screening for the desired antibody can be accomplished by techniques known in the art, *e.g.*, ELISA (enzyme-linked immunosorbent assay). To select antibodies specific to a particular domain of a biomarker or derivatives, homologs, or analogs thereof, one may assay generated hybridomas for a product that binds to the fragment of the a biomarker, that contains such a domain.

An "epitope", as used herein, is a portion of a polypeptide that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Epitopes may generally be identified using well known techniques, such as those summarized in Paul, Fundamental Immunology, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides derived from the native polypeptide for the ability to react with antigen-specific antisera and/or T-cell lines or clones. An epitope of a polypeptide is a portion that reacts with such antisera and/or T-cells at a level that is similar to the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such screens may generally be performed using methods well known to those of ordinary skill

in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. B-cell and T-cell epitopes may also be predicted via computer analysis. Polypeptides comprising an epitope of a polypeptide that is preferentially expressed in a tumor tissue (with or without additional amino acid sequence) are within the scope of the present invention.

Methods for detecting the expression of a protein biomarker may also include extracting the protein contents of the cells, or extracting fragments of protein from the membranes of the cells, or from the cytosol, for example, by lysis, digestive, separation, fractionation and purification techniques, and separating the proteinaceous contents of the cells (either the crude contents or the purified contents) on a western blot, and then detecting the presence of the protein, or protein fragment by various identification techniques known in the art. For example, the contents separated on a gel may be identified by using suitable molecular weight markers together with a protein identification technique, or using suitable detecting moieties (such as labeled antibodies, labeled lectins, labeled binding agents (agonists, antagonists, substrates, co-factors, ATP, etc.).

Antibodies useful in the techniques of the invention and, for example, specific for the biomarkers listed in Table 9 may be available commercially or made by one of skill in the art. These antibodies are useful in the methods described. For example, one or more of these antibodies, as well as one or more of the antibodies generated to the biomarkers, may be part of an antibody array. Such an antibody array can be used to screen samples from subjects as described herein for diagnostic and screenings purposes. Manufacturer information on candidate antibodies to the discordant genes is available at <http://www.linscottsdirectory.com>. Based on the database Immunoquery (<http://www.Immunoquery.com>). Each marker has the diagnosis to which it is linked, number of positives found and total number of cases in it was used for diagnosis.

#### **Diagnosis Of Subject And Determination Of Renal Status**

Any biomarker (e.g., the discordantly expressed transcripts listed in Tables 5 – 20, and 11) individually, is useful in aiding in the determination of renal status. First, the selected biomarker is measured in a subject sample using the methods described herein, e.g., capture on a nucleic acid microarray followed by detection. Then, the measurement is compared with a diagnostic amount or control that distinguishes renal status, e.g., injured, cancerous or normal renal status. The diagnostic amount will reflect the information herein that a particular biomarker is up-regulated or down-regulated in a cancer status compared with a non-cancer status. As is well understood in the art, the particular diagnostic amount used can be adjusted

to increase sensitivity or specificity of the diagnostic assay depending on the preference of the diagnostician. The test amount as compared with the diagnostic amount thus indicates renal status.

In one embodiment, biomarkers include for example, discordant genes (e.g., down-regulated in RRR and up-regulated in RRC. Discordant biomarkers for RRR, include, for example any one or more of, or a combination of, IGFBP1, IGFBP3, CTGF, AKT, FRAP, MYC, NF- $\kappa$ B, HK1 and SIRT7. In one embodiment, biomarker for RRR comprise, for example, IGFBP1 and IGFBP3; IGFBP1 and CTGF; IGFBP1 and AKT; IGFBP1 and FRAP; IGFBP1 and MYC; IGFBP1 and NF- $\kappa$ B; IGFBP1 and HK1; IGFBP1 and SIRT7; IGFBP1, IGFBP3 and CTGF; IGFBP1, IGFBP3 and AKT; CTGF, AKT, FRAP, MYC, NF- $\kappa$ B, HK1 and SIRT7 FRAP; IGFBP1, IGFBP3 and MYC; IGFBP1, IGFBP3 and NF- $\kappa$ B; IGFBP1, IGFBP3 and HK1; IGFBP1, IGFBP3 and SIRT7; and other combinations. In one embodiment, a biomarker of RRC comprises HK1, which is upregulated in RRC and down-regulated in RRR.

While individual biomarkers are useful diagnostic markers, it has been found that a combination of biomarkers provides greater predictive value than single markers alone. Specifically, the detection of a plurality of markers in a sample increases the percentage of true positive and true negative diagnoses and would decrease the percentage of false positive or false negative diagnoses. Thus, preferred methods of the present invention comprise the measurement of more than one biomarker. For example, measuring two or more markers from one or more clusters of markers.

In some embodiments, the mere presence or absence of a marker, without quantifying the amount of marker, is useful and can be correlated with a probable diagnosis of renal cancer. For example, Table 8 lists the times specific biomarkers are expressed in RRR and RCC cells. Thus, the detection of a particular biomarker is indicative of that cell's status and a detected presence or absence, respectively, of these markers in a subject being tested indicates that the subject has a higher probability of having renal cancer.

In other embodiments, the measurement of markers can involve quantifying the markers to correlate the detection of markers with a probable diagnosis of renal cancer. Thus, if the amount of the markers detected in a subject being tested is different compared to a control amount (i.e., higher or lower than the control, depending on the marker), then the subject being tested has a higher probability of having renal cancer.

The correlation may take into account the amount of the marker or markers in the sample compared to a control amount of the marker or markers (up or down regulation of the marker or markers) (e.g., in normal subjects in whom human cancer is undetectable). A control can be, e.g., the average or median amount of marker present in comparable samples of normal subjects in whom human cancer is undetectable. The control amount is measured under the same or substantially similar experimental conditions as in measuring the test amount. The correlation may take into account the presence or absence of the markers in a test sample and the frequency of detection of the same markers in a control. The correlation may take into account both of such factors to facilitate determination of renal status.

In certain embodiments of the methods of qualifying renal status, the methods further comprise managing subject treatment based on the status. As aforesaid, such management describes the actions of the physician or clinician subsequent to determining renal status. For example, if the result of the methods of the present invention is inconclusive or there is reason that confirmation of status is necessary, the physician may order more tests. Alternatively, if the status indicates that surgery is appropriate, the physician may schedule the patient for surgery. In other instances, the patient may receive chemotherapy or radiation treatments, either in lieu of, or in addition to, surgery. Likewise, if the result is negative, e.g., the status indicates late stage renal cancer or if the status is otherwise acute, no further action may be warranted. Furthermore, if the results show that treatment has been successful, no further management may be necessary.

The invention also provides for such methods where the biomarkers (or specific combination of biomarkers) are measured again after subject management. In these cases, the methods are used to monitor the status of the cancer, e.g., response to cancer treatment, remission of the disease or progression of the disease. Because of the ease of use of the methods and the lack of invasiveness of the methods, the methods can be repeated after each treatment the patient receives. This allows the physician to follow the effectiveness of the course of treatment. If the results show that the treatment is not effective, the course of treatment can be altered accordingly. This enables the physician to be flexible in the treatment options.

In another example, the methods for detecting markers can be used to assay for and to identify compounds that modulate expression of these markers *in vivo* or *in vitro*.

The methods of the present invention have other applications as well. For example, the markers can be used to screen for compounds that modulate the expression of the markers *in vitro* or *in vivo*, which compounds in turn may be useful in treating or preventing renal

cancer in patients. In another example, the markers can be used to monitor the response to treatments for renal cancer. In yet another example, the markers can be used in heredity studies to determine if the subject is at risk for developing renal cancer. For instance, certain markers may be genetically linked. This can be determined by, *e.g.*, analyzing samples from a population of renal cancer patients whose families have a history of renal cancer. The results can then be compared with data obtained from, *e.g.*, renal cancer patients whose families do not have a history of renal cancer. The markers that are genetically linked may be used as a tool to determine if a subject whose family has a history of renal cancer is pre-disposed to having renal cancer.

Additional embodiments of the invention relate to the communication of assay results or diagnoses or both to technicians, physicians or patients, for example. In certain embodiments, computers will be used to communicate assay results or diagnoses or both to interested parties, *e.g.*, physicians and their patients. In some embodiments, the assays will be performed or the assay results analyzed in a country or jurisdiction which differs from the country or jurisdiction to which the results or diagnoses are communicated.

In a preferred embodiment of the invention, a diagnosis based on the presence or absence in a test subject of any the biomarkers of this invention is communicated to the subject as soon as possible after the diagnosis is obtained. The diagnosis may be communicated to the subject by the subject's treating physician. Alternatively, the diagnosis may be sent to a test subject by email or communicated to the subject by phone. A computer may be used to communicate the diagnosis by email or phone. In certain embodiments, the message containing results of a diagnostic test may be generated and delivered automatically to the subject using a combination of computer hardware and software which will be familiar to artisans skilled in telecommunications. One example of a healthcare-oriented communications system is described in U.S. Patent Number 6,283,761; however, the present invention is not limited to methods which utilize this particular communications system. In certain embodiments of the methods of the invention, all or some of the method steps, including the assaying of samples, diagnosing of diseases, and communicating of assay results or diagnoses, may be carried out in diverse (*e.g.*, foreign) jurisdictions.

The term diagnosis as used herein generally comprises any kind of assessment of the presence or absence of a medically relevant condition. Diagnosis thus comprises processes such as screening for the predisposition for a medically relevant condition, screening for the precursor of a medically relevant condition, screening for a medically relevant condition, clinical or pathological diagnosis of a medically relevant condition, etc. Diagnosis of

medically relevant conditions as used herein may comprise examination of any condition, that is detectable on a cytological, histological, biochemical or molecular biological level, that may be useful in respect to the human health and/or body. Such examinations may comprise e.g., medical diagnostic methods and research studies in life sciences. In one embodiment of the invention, the method is used for diagnosis of medically relevant conditions such as e.g., diseases. Such diseases may for example comprise disorders characterized by proliferation of cells or tissues.

In one embodiment, the diagnosis pertains to diagnosis of cancers and their precursory stages, to monitoring of the disease course in cancers, to assessment of prognosis in cancers and to detection of disseminated tumor cells, e.g., in the course of minimal residual disease diagnosis. The methods according to the present invention may for example be used in the course of clinical or pathological diagnosis of cancers and their precursory stages or in routine screening tests as performed for particular cancers such as for example for examination of swabs e.g. in screening tests for renal cancer.

One aspect of this normalization includes comparing the results of a determination of one or more of the parameters disclosed herein and determining one or more of the cellular expression pattern of a biomarker.

Correlating may include making an assessment that a particular result is not accurate. Correlating may also include predicting whether a certain marker is a meaningful in the context of diagnosis, prognosis, and/or monitoring of treatment. Correlating may be done by mathematical formulae, computer program, or a person. As disclosed herein, certain markers are predictive of disease state or progression of disease state. Correlating or normalization, especially in the context of a diagnosis, may also include or take into consideration, such factors as, the total number of cells present in the sample, of the presence or absence of a particular cell type or types in a sample, the presence or absence of an organism or of cells of an organism in a sample, the number of cells of a particular cell type or organism present in the sample, the proliferative characteristics of cells present in the sample, or the differentiation pattern of the cells present in the sample.

In certain embodiments normalization may also comprise demonstrating the adequacy of the test, wherein as the case may be inadequate test results may be discarded or classified as invalid. Therefore normalization as used in the context of the present invention may comprise qualitative or semi-quantitative methods for normalization. In certain embodiments, semi-quantitative normalization may comprise determining a threshold value for a normalization marker.

## Therapeutic Candidates and Methods of Treatment

The methods of the present invention have other applications as well. For example, the biomarkers can be used to screen for compounds that modulate the expression of the biomarkers in vitro or in vivo, which compounds in turn may be useful in treating or preventing renal cancer in patients. In another example, the biomarkers can be used to monitor the response to treatments for renal cancer. In yet another example, the biomarkers can be used in heredity studies to determine if the subject is at risk for developing renal cancer.

Thus, for example, the kits of this invention could include a solid substrate, such as a nucleic acid biochip and a buffer for washing the substrate, as well as instructions providing a protocol to measure the biomarkers of this invention on the chip and to use these measurements to diagnose renal cancer.

Based on the results of the analysis, identified among the concordant and discordant genes and other genes in their pathways, were compounds that could be used as gene-drug targets. The pharmaceutical composition identified through the screening methods of the invention may be given in combination. Useful combinations of therapeutics will offer one or more of the following improvements over a single composition therapeutic: improve the efficacy of one or more of the therapeutics in the composition, lower the dosage of one or more of the therapeutics in the composition, decrease the time of action of one or more of the therapeutics in the composition, decrease the toxicity of one or more of the therapeutics in the composition. Therapeutics that may be given in combination include the therapeutics identified by, linked or generated by the software program and database as PharmaProjects as well as the therapeutics identified in the screening methods of the invention. The therapeutics can be used to treat, for example, RCC, acute renal failure, RRR, organ transplantation, organ shipment, wound healing, other tumors and organ failure.

Compounds suitable for therapeutic testing may be screened initially, for example, by identifying compounds which interact with one or more biomarkers listed in identified herein or compounds that are known to interact with a biomarker.

In a related embodiment, the ability of a test compound to alter the expression profile of one or more of the biomarkers of this invention may be measured. One of skill in the art will recognize that the techniques used to measure the expression profile of a particular biomarker will vary depending on the function and properties of the biomarker. For example, an enzymatic activity of a biomarker may be assayed provided that an appropriate substrate is

available and provided that the concentration of the substrate or the appearance of the reaction product is readily measurable. The ability of potentially therapeutic test compounds to inhibit or enhance the expression profile of a given biomarker may be determined by measuring the rates of catalysis in the presence or absence of the test compounds. The ability of a test

5 compound to interfere with a non-enzymatic (e.g., structural) function or expression profile of one of the biomarkers of this invention may also be measured. For example, the self-assembly of a multi-protein complex which includes one of the biomarkers of this invention may be monitored by spectroscopy in the presence or absence of a test compound. Alternatively, if the biomarker is a non-enzymatic enhancer of transcription, test compounds which interfere  
10 with the ability of the biomarker to enhance transcription may be identified by measuring the expression patterns of biomarker-dependent transcription in vivo or in vitro in the presence and absence of the test compound. Test compounds capable of modulating the expression profile of any of the biomarkers of this invention may be administered to patients who are suffering from or are at risk of developing renal carcinoma or other cancer. For example, the  
15 administration of a test compound which alters the expression profile of a discordantly expressed marker may decrease the risk of renal cancer in a patient.

In yet another embodiment, the invention provides a method for treating or reducing the progression or likelihood of a disease, e.g., renal carcinoma. For example, after one or more markers have been identified which are predictive of the state of a sample, e.g., whether  
20 the sample is benign, is in the initiation phase, extension phase, maintenance phase, or is carcinoma, combinatorial libraries may be screened for compounds which alter the expression profile of the markers toward a normal or health, or regeneration and/or repair profile.

Methods of screening chemical libraries for such compounds are well-known in art. See, e.g., Lopez-Otin et al. (2002). At the clinical level, screening a test compound includes obtaining  
25 samples from test subjects before and after the subjects have been exposed to a test compound. The expression patterns in the samples of one or more of the biomarkers of this invention may be measured and analyzed to determine whether the expression patterns of the biomarkers change after exposure to a test compound. The samples may be analyzed by mass  
spectrometry, as described herein, or the samples may be analyzed by any appropriate means

30 known to one of skill in the art. For example, the expression patterns of one or more of the biomarkers of this invention may be measured directly by Western blot using radio- or fluorescently-labeled antibodies which specifically bind to the biomarkers. Alternatively, changes in the expression patterns of mRNA encoding the one or more biomarkers may be measured and correlated with the administration of a given test compound to a subject. In a  
35 further embodiment, the changes in the expression pattern of expression of one or more of the



biomarkers may be measured using in vitro methods and materials. For example, human tissue cultured cells which express, or are capable of expressing, one or more of the biomarkers of this invention may be contacted with test compounds. Subjects who have been treated with test compounds will be routinely examined for any physiological effects which may result from the treatment. In particular, the test compounds will be evaluated for their ability to decrease disease likelihood in a subject. Alternatively, if the test compounds are administered to subjects who have previously been diagnosed with renal cancer, test compounds will be screened for their ability to slow or stop the progression of the disease. For protein biochips, test compounds would then be contacted with the substrate, typically in aqueous conditions, and interactions between the test compound and the biomarker are measured, for example, by measuring elution rates as a function of salt concentration. Certain proteins may recognize and cleave one or more biomarkers of this invention, in which case the proteins may be detected by monitoring the digestion of one or more biomarkers in a standard assay, e.g., by gel electrophoresis of the proteins.

The invention provides methods for identifying modulators, i.e., candidate or test compounds or agents (e.g. peptides, small molecules or other drugs) that have a stimulatory or inhibitory effect on the pathway(s) affected by the agent and have anti-proliferative properties. Such compounds may include, but are not limited to, peptides made of D-and/or L-configuration amino acids (in, for example, the form of random peptide libraries; (see e.g., Lam, et al., *Nature*, 354:82-4 (1991)), phosphopeptides (in, for example, the form of random or partially degenerate, directed phosphopeptide libraries; see, e.g., Songyang, et al., *Cell*, 72:767-78 (1993)), antibodies, and small organic or inorganic molecules. Compounds identified may be useful, for example, in modulating the activity of a biomarker pathway biomarker gene proteins, (e.g., cellular expression pattern of RXR-alpha).

In one embodiment, the invention provides libraries of test compounds. The test compounds of the present invention can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries, spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the one-bead one-compound library method; and synthetic library methods using affinity chromatography selection. The biological library approach is exemplified by peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds (Lam, K. S. (1997) "Application of combinatorial library methods in cancer research and drug discovery." *Anticancer Drug Des.* 12:145).

Methods for the synthesis of molecular libraries can be found in the art, for example, in (i) De Witt, S. H. et al. (1993) "Diversomers: an approach to nonpeptide, nonoligomeric chemical diversity." PNAS 90:6909, (ii) Erb, E. et al. (1994) "Recursive deconvolution of combinatorial chemical libraries." PNAS 91:11422, (iii) Zuckermann, R. N. et al. (1994)

5 "Discovery of nanomolar ligands for 7-transmembrane G-protein-coupled receptors from a diverse N-(substituted)glycine peptide library." J. Med Chem. 37: 2678 and (iv) Cho, C. Y. et al. (1993) "An unnatural biopolymer." Science 261:1303. Libraries of compounds may be presented in i) solution (e.g. Houghten, R. A. (1992) "The use of synthetic peptide combinatorial libraries for the identification of bioactive peptides." BioTechniques 13:412) ii) 10 on beads (Lam, K. S. (1991) "A new type of synthetic peptide library for identifying ligand-binding activity." Nature 354:82), iii) chips (Fodor, S. P. (1993) "Multiplexed biochemical assays with biological chips." Nature 364:555), iv) bacteria (U.S. Pat. No. 5,223,409), v) spores (U.S. Pat. Nos. 5,571,698, 5,403,484, and 5,223,409), vi) plasmids (Cull, M. G. et al. (1992) "Screening for receptor ligands using large libraries of peptides linked to the C 15 terminus of the lac repressor." PNAS 89:1865) or vii) phage (Scott, J. K. and Smith, G. P. (1990) "Searching for peptide ligands with an epitope library." Science 249: 386)

The practice of the present invention employs, unless otherwise indicated, conventional molecular biology, microbiology, and recombinant DNA techniques within the skill of the art. Such techniques are explained fully in the literature. See, e.g., Maniatis, 20 Fritsch & Sambrook, In Molecular Cloning: A Laboratory Manual (1982); DNA Cloning: A Practical Approach, Volumes I and II, D. N. Glover, ed., (1985); Oligonucleotide Synthesis, M. J. Gait, ed., (1984); Ausubel, et al., (eds.), Current Protocols In Molecular Biology, John Wiley & Sons, New York, N.Y. (1993); Nucleic Acid Hybridization, B. D. Hames & S. J. Higgins, eds., (1985); Transcription and Translation, B. D. Hames & S. I. Higgins, eds., 25 (1984); Animal Cell Culture, R. I. Freshney, ed. (1986); and B. Perbal, A Practical Guide to Molecular Cloning (1984).

As used herein, "comparing" in relation to "cellular expression pattern of a biomarker refers to making an assessment of the how the cellular expression pattern of a sample relates to the cellular expression pattern of the standard. For example, assessing whether the cellular 30 expression pattern of the sample is different from the cellular expression pattern of the standard cellular expression pattern, for example of a reference cell as described herein.

In a particular embodiment, the present invention provides a method for treating a disease or disorder characterized by aberrant cellular expression pattern of a biomarker comprising administering to a subject having such disease or disorder a composition

comprising a molecule that alters the subcellular expression pattern of a biomarker and a pharmaceutically acceptable carrier.

Once obtained, the results of any assay herein may be reported to the subject or a health care professional, e.g., reporting the cellular expression pattern of a biomarker. The report to the subject may also be accompanied by a diagnosis and recommendations for treatment.

Following diagnosis or assessment of likelihood of an efficacious result, the treatment may include surgery, focal therapy (mucosectomy, argon plasma coagulator, cryotherapy), selenium fortification, chemoradiation therapy, chemotherapy, radiotherapy, including but not limited to, tamoxifen, trastuzumab (herceptin), raloxifene, doxorubicin, fluorouracil/5-flu, pamidronate disodium, anastrozole, exemestane, cyclophosphamide, epirubicin, letrozole, toremifene, fulvestrant, fluoxymesterone, trastuzumab, methotrexate, megastrol acetate, docetaxel, paclitaxel, testolactone, aziridine, vinblastine, capecitabine, goserelin acetate, zoledronic acid, taxol. The appropriate treatment for a particular subject may be determined by one of skill in the art.

The identification of those patients who are in need of prophylactic treatment for cancer is well within the ability and knowledge of one skilled in the art. Certain of the methods for identification of patients which are at risk of developing cancer which can be treated by the subject method are appreciated in the medical arts, such as family history, travel history and expected travel plans, the presence of risk factors associated with the development of that disease state in the subject patient. A clinician skilled in the art can readily identify such candidate patients, by the use of, for example, clinical tests, physical examination and medical/family/travel history. Risk factors for renal cancer include aging, family history, a previous history of renal cancer, having had radiation therapy to the chest region, being Caucasian, menstruating prior to the age of 12, late menopause (after age 50), long term hormone replacement therapy, nulliparity, having children after the age of 30, and/or genetic mutations.

"After an initial period of treatment" or after an appropriate period of time after the administration of the therapeutic, e.g., 2 hours, 4 hours, 8 hours, 12 hours, or 72 hours, one or more of the cellular expression patterns may be determined again. The modulation of one or more of the cellular expression patterns may indicate efficacy of an anti-cancer treatment. One or more of the cellular expression patterns may be determined periodically throughout treatment. For example, one or more of the cellular expression patterns may be checked every few hours, days or weeks to assess the further efficacy of the treatment. The method described

may be used to screen or select patients that may benefit from treatment with a therapeutic or related therapy.

The initial period of treatment may be the time required to achieve a steady-state plasma or cellular concentration of the therapeutic or related cancer treatment. The initial  
5 period may also be the time to achieve a modulation in one or more cellular expression patterns.

Treatment of a subject may entail administering more than one dose of a therapeutic in a therapeutically effective amount. Between doses, it may be desirable to determine one or more of the cellular expression patterns in the tumor after a second period of treatment with  
10 the therapeutic or related cancer treatment. This is one example how a treatment course may be monitored to determine if it continues to be efficacious for the subject when monitoring the treatment, it may be desirable to comparing one or more of the pre-treatment or post-treatment cellular expression patterns to a standard cellular expression pattern.

The present invention presents methods of treating a subject identified with renal  
15 cancer. The identification may be by diagnosis as described herein or by self-identification. The diagnosis of renal cancer may be, for example, by clinical examination, imaging procedures (e.g., ultrasound, magnetic resonance imaging (MRI)), and/or biopsy (surgical removal of tissue for microscopic examination) of a mass detected by physical examination.

A subject in need treatment for renal cancer may be treated by co-administering,  
20 radiation agent, biological agent (stem cell, antibody) or an anti-inflammatory agent to the subject. Chemotherapeutic agents may include an agent identified through the screening methods described herein, one or more of the agents linked or generated by a software program and database as PharmaProjects, or other agent determined by a health care professional.

Methods of monitoring the treatment of a subject for renal carcinoma, include,  
25 determining a pre-treatment cellular marker expression profile a cell of a subject; administering a therapeutically effective amount of a candidate compound, and determining a post-treatment cellular marker expression profile in a cell of a subject. A modulation of the a biomarker expression pattern indicates the efficacy of treatment with the a biomarker C-  
30 terminal peptide. Additional steps may also include, identifying a subject that may be retinoid unresponsive, diagnosing a subject with renal carcinoma, renal ischemia, acute renal failure, RRR, graft, and/or a subject in need of renal transplantation, and/or obtaining a cell sample from the subject.

"Cellular marker expression profile," "pattern of expression" "expression profile" refer to determining whether or not one or more of a biomarker is expressed in a cell at a particular time, for example, pre-treatment, during treatment, or after treatment.

A method, according to the invention, to assess whether a subject who has cancer is likely to exhibit a favorable clinical response to treatment with an a biomarker therapeutic, for example, a candidate compound, comprises determining a pre-treatment expression profile of one or more biomarkers in a cell of a subject, administering a therapeutically effective amount of a candidate compound, and determining a post-treatment expression profile of the one or more biomarkers in a cell of a subject. A modulation of the a biomarker expression or the stasis of the biomarker profile following administration is an indication that the cancer is likely to have a favorable clinical response to treatment with a candidate compound.

The method of assessing whether a subject who has cancer is likely to exhibit a favorable clinical response may further comprise comparing one or more of the pre-treatment or post-treatment expression patterns of a biomarker to a standard a biomarker expression pattern. The standard a biomarker expression pattern may be the corresponding a biomarker expression pattern in a reference cell or population of cells or from normal tissue surrounding suspected cancerous tissue, or tissue from another portion of the subject, including a kidney not suspected of being cancerous.

A reference cell may be one or more of the following, cells from the subject, cultured cells, cultured cells from the subject, or cells from the subject pre-treatment. The cells may be cells from normal tissue surrounding suspected cancerous tissue, or tissue from another portion of the subject, including a kidney not suspected of being cancerous.

As used herein, "a reference cell or population of cells" refers to a cell sample that is clinically normal, clinically somewhere on the continuum between normal and neoplastic, or is neoplastic, depending on the particular methods of use. The reference cell may be one or more of the following, cells from the subject, cultured cells, cultured cells from the subject, or cells from the subject pre-treatment, for example, a sample from a different portion of the tissue being diagnosed, or it may a from another tissue of the subject. The cells may alternately be from the subject post-treatment. The reference may also be from treated tissue culture cells. The cultures may be primary or established cultures and may be from the subject being diagnosed or from another source. The cultures may be from the same tissue being diagnosed or from another tissue. The cultures may also be normal, anywhere on the continuum from normal to neoplastic, and/or neoplastic. For example, a reference cell may be a cell from the normal kidney of a subject with renal cancer.

Methods of treating renal cancer in a subject, according to the invention, include, administering a therapeutically effective amount of a candidate compound to a subject diagnosed with cancer.

The renal cancer may be at any one or more of the stages identified by a cancer staging system. A staging system is a standardized way in which the cancer care team describes the extent of the cancer. The most commonly used staging system is that of the American Joint Committee on Cancer (AJCC), sometimes also known as the TNM system ([www.cancer.gov](http://www.cancer.gov)):

Screening methods, according to the invention, to identify candidate molecules to treat renal cancer, comprise contacting a cell, e.g., a cancerous cell or an ischemically injured cell, with a candidate molecule; an detecting expression pattern of a biomarker the cell, wherein expression pattern of the a biomarker in a pattern according to Table 9 indicates the molecule may be useful to treat renal cancer. Alternately, correlating the expression pattern with the patterns indicated in Table 9 indicates the renal status. The candidate molecule may be one or more of a small molecule, a peptide, or a nucleic acid. Screening methods may further comprise comparing the expression pattern to a standard expression pattern, e.g., the corresponding expression pattern in a reference cell or population of cells. A reference cell may be one or more cells from the subject, cultured cells, cultured cells from the subject, or cells from the subject pre-treatment, or a cell sample as described herein.

As used herein, "renal therapeutic," "renal related cancer therapeutic," "renal related cancer therapeutic," and "Therapeutic," are used interchangeably to indicate a compound, peptide, or other agent that is useful to treat, prevent or ameliorate renal carcinoma.

The present invention is further directed to the compounds identified by the above-described screening assays and to processes for producing such agents by use of these assays. In a preferred aspect, the renal therapeutic is substantially purified. The compounds can include, but are not limited to, nucleic acids, antisense nucleic acids, ribozyme, triple helix, antibody, and polypeptide molecules and small inorganic or organic molecules. Accordingly, in one embodiment, the present invention includes a compound obtained by a method comprising the steps of any one of the aforementioned screening assays. For example, the compound is obtained by a method comprising contacting a cell with one or more candidate molecules; and detecting expression pattern of a biomarker in the cell.

Once a test compound has been identified as having an appropriate activity according to the screening methods of the present invention, the test compound can be subject to further testing, for example, in animal models to confirm its activity as a renal related therapeutic.

The test compound can also be tested against known compounds that modulate one of the parameters, in cell based or animal assays, to confirm its desired activity. The identified compound can also be tested to determine its toxicity, or side effects that could be associated with administration of such compound. Alternatively, a compound identified as described herein can be used in an animal model to determine the mechanism of action of such a compound.

The genes expressed concordantly in RRR and RCC may permit the tumor to respond to certain physiological signals that are known inhibit tissue regeneration. Therapeutic agents similar to such signaling molecules (i.e., initiation of DNA replication) could be developed and tested in the screening assays described herein .

### Cloning of Biomarkers

The term "vector" refers to a nucleotide sequence that can assimilate new nucleic acids, and propagate those new sequences in an appropriate host. Vectors include, but are not limited to recombinant plasmids and viruses. The vector (e.g., plasmid or recombinant virus) comprising the nucleic acid of the invention can be in a carrier, for example, a plasmid complexed to protein, a plasmid complexed with lipid-based nucleic acid transduction systems, or other non-viral carrier systems.

A broad variety of suitable microbial vectors are available. Generally, a microbial vector will contain an origin of replication recognized by the intended host, a promoter which will function in the host and a phenotypic selection gene such as a gene encoding proteins conferring antibiotic resistance or supplying an autotrophic requirement. Similar constructs will be manufactured for other hosts. *E. coli* is typically transformed using pBR322. See Bolivar et al., Gene 2, 95 (1977). The vector pBR322 contains genes for ampicillin and tetracycline resistance and thus provides easy means for identifying transformed cells. Expression vectors should contain a promoter which is recognized by the host organism. This generally means a promoter obtained from the intended host. Promoters most commonly used in recombinant microbial expression vectors include the beta-lactamase (penicillinase) and lactose promoter systems (Chang et al., Nature 275, 615 (1978); and Goeddel et al., Nucleic Acids Res. 8, 4057 (1980) and EPO Application Publication Number 36,776) and the *tac* promoter (H. De Boer et al., Proc. Natl. Acad. Sci. USA 80, 21 (1983)).

The isolated nucleotide sequences of the invention may be cloned or subcloned using any method known in the art (See, for example, Sambrook, J. et al., Molecular Cloning, Cold Spring Harbor Press, New York, 1989), the entire contents of which are incorporated herein

by reference. In particular, nucleotide sequences of the invention may be cloned into any of a large variety of vectors. Possible vectors include, but are not limited to, cosmids, plasmids or modified viruses, although the vector system must be compatible with the host cell used.

Viral vectors include, but are not limited to, lambda, simian virus, bovine papillomavirus,

- 5 Epstein-Barr virus, and vaccinia virus. Viral vectors also include retroviral vectors, such as Amphatrophic Murine Retrovirus (see Miller et al., *Biotechniques*, 7:980-990 (1984)), incorporated herein by reference). Plasmids include, but are not limited to, pBR, PUC, pGEM (Promega), and Bluescript Registered TM (Stratagene) plasmid derivatives. Introduction into and expression in host cells is done for example by, transformation, transfection, infection, electroporation, etc.

Conventional procedures were also used to make vector DNA, cleave DNA with restriction enzymes, ligate and purify DNA, transform and/or transfect host cells, culture the host cells, and isolate and purify proteins and polypeptides. See generally Sambrook et al., *Molecular Cloning* (2d ed. 1989), and Ausubel et al. *supra*. Examples of cells which can express isolated DNAs encoding the antibodies disclosed herein include bacterial cells (e.g., *E. coli* and *B. subtilis*) such as, e.g., MM294, DM52, XL1-blue (Stratagene), animal cells (e.g., NSO, CV-1, CHO cells), yeast cells (e.g., *S. cerevisiae*), amphibian cells (e.g., *Xenopus oocyte*), and insect cells (e.g., *Spodoptera frugiperda* or *Trichoplusia ni*). Methods of expressing recombinant DNA in these cells are known, e.g., see Sambrook et al., *Molecular Cloning* (2d ed. 1989), Ausubel et al. *supra*, and Summer and Smith, *A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures: Texas Agricultural Experimental Station Bulletin No. 1555*, College Station Texas (1988).

- A vector, according to the invention, may contain a polynucleotide capable of encoding a polypeptide having at least about 80% sequence identity to the sequences, and characterized by the ability to alter the expression pattern of a biomarker. The encoded polypeptide may also be at least 85%, 90%, 95%, or 99.9% identical to at least one of the sequences identified herein. A vector according to the invention may encode more than one polynucleotide capable of encoding a peptide characterized by he ability to alter the expression pattern of a biomarker, for example, the vector may encode two, three or four polynucleotides capable of encoding a peptide characterized by he ability to alter the expression pattern of a biomarker.

Preferably the a biomarker polynucleotide of the invention is derived from a mammalian organism, and most preferably from human. Screening procedures which rely on nucleic acid hybridization make it possible to isolate any gene sequence from any organism,



provided the appropriate probe is available. Oligonucleotide probes, which correspond to a part of the sequence encoding the protein in question, can be synthesized chemically. This requires that short, oligopeptide stretches of amino acid sequence must be known. The DNA sequence encoding the protein can be deduced from the genetic code., however, the degeneracy of the code must be taken into account. It is possible to perform a mixed addition reaction when the sequence is degenerate. This includes a heterogeneous mixture of denatured double-stranded DNA. For such screening, hybridization is preferably performed on either single-stranded DNA or denatured double-stranded DNA. Hybridization is particularly useful in the detection of cDNA clones derived from sources where an extremely low amount of mRNA sequences relating to the polypeptide of interest are present. In other words, by using stringent hybridization conditions directed to avoid non-specific binding, it is possible, for example, to allow the autoradiographic visualization of a specific cDNA clone by the hybridization of the biomarker DNA to that single probe in the mixture which is its complete complement (Wallace, et al., Nucl. Acid Res., 9:879, 1981; Maniatis, et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor, N.Y. 1989).

The development of specific DNA sequences encoding a biomarker can also be obtained by: 1) isolation of double-stranded DNA sequences from the genomic DNA; 2) chemical manufacture of a DNA sequence to provide the necessary codons for the polypeptide of interest; and 3) in vitro synthesis of a double-stranded DNA sequence by reverse transcription of mRNA isolated from a eukaryotic donor cell. In the latter case, a double-stranded DNA complement of mRNA is eventually formed which is generally referred to as cDNA.

DNA sequences encoding a biomarker can be expressed in vitro by DNA transfer into a suitable host cell. "Host cells" are cells in which a vector can be propagated and its DNA expressed. The term also includes any progeny of the subject host cell. It is understood that all progeny may not be identical to the parental cell since there may be mutations that occur during replication. However, such progeny are included when the term "host cell" is used. Methods of stable transfer, meaning that the foreign DNA is continuously maintained in the host, are known in the art.

Polynucleotide sequences encoding a biomarker can be expressed in either prokaryotes or eukaryotes. Hosts can include microbial, yeast, insect and mammalian organisms. Methods of expressing DNA sequences having eukaryotic or viral sequences in prokaryotes are well known in the art. Biologically functional viral and plasmid DNA vectors capable of expression and replication in a host are known in the art. Such vectors are used to incorporate

DNA sequences of the invention. Transformation of a host cell with recombinant DNA may be carried out by conventional techniques as are well known to those skilled in the art. Where the host is prokaryotic, such as *E. coli*, competent cells which are capable of DNA uptake can be prepared from cells harvested after exponential growth phase and subsequently treated by the  $\text{CaCl}_2$  method using procedures well known in the art. Alternatively,  $\text{MgCl}_2$  or  $\text{RbCl}$  can be used. Transformation can also be performed after forming a protoplast of the host cell if desired. Isolation and purification of microbial expressed polypeptide, or fragments thereof, provided by the invention, may be carried out by conventional means including preparative chromatography and immunological separations involving monoclonal or polyclonal antibodies. The a biomarker polypeptides of the invention can also be used to produce antibodies which are immunoreactive or bind to epitopes of the a biomarker polypeptides. Antibody which consists essentially of pooled monoclonal antibodies with different epitopic specificities, as well as distinct monoclonal antibody preparations are provided. Monoclonal antibodies are made from antigen containing fragments of the protein by methods well known in the art (Kohler, et al., *Nature*, 256:495, 1975; *Current Protocols in Molecular Biology*, Ausubel, et al., ed., 1989).

The identification of a novel member of the a biomarker family may provide useful tools for diagnosis, prognosis and therapeutic strategies associated with a biomarker mediated disorders. Methods of identifying a biomarker family members are well known to one of skill in the art.

### **Pharmaceutical Compositions**

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of at least one therapeutic, (e.g., a renal related therapeutic), and a pharmaceutically acceptable carrier.

In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly, in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the renal related therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water can be a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are

preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain  
5 minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch,  
10 magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the  
15 mode of administration.

In a preferred embodiment, the composition is formulated, in accordance with routine procedures, as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a  
20 local anesthetic such as lidocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water-free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile  
25 pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water or saline for injection can be provided so that the ingredients may be mixed prior to administration.

The therapeutics of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free carboxyl groups such as  
30 those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., those formed with free amine groups such as those derived from isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc., and those derived from sodium, potassium, ammonium, calcium, and ferric hydroxides, etc.

Preferred pharmaceutical compositions and dosage forms comprise a therapeutic of the invention, or a pharmaceutically acceptable prodrug, salt, solvate, or clathrate thereof, optionally in combination with one or more additional active agents.

The amount of the therapeutic of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, *in vitro* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, suitable dosage ranges for intravenous administration are generally about 1-50 milligrams of active compound per kilogram body weight. Suitable dosage ranges for intranasal administration are generally about 0.1 mg/kg body weight to 50 mg/kg body weight. Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

Suppositories generally contain active ingredient in the range of 0.5% to 10% by weight; oral formulations preferably contain 10% to 95% active ingredient.

Exemplary doses of a small molecule include milligram or microgram amounts of the small molecule per kilogram of subject or sample weight (*e.g.*, about 1 microgram per kilogram to about 500 milligrams per kilogram, about 100 micrograms per kilogram to about 5 milligrams per kilogram, or about 1 microgram per kilogram to about 50 micrograms per kilogram).

For antibodies, proteins, polypeptides, peptides and fusion proteins encompassed by the invention, the dosage administered to a patient is typically 0.0001 mg/kg to 100 mg/kg of the patient's body weight. Preferably, the dosage administered to a patient is between 0.0001 mg/kg and 20 mg/kg, 0.0001 mg/kg and 10 mg/kg, 0.0001 mg/kg and 5 mg/kg, 0.0001 and 2 mg/kg, 0.0001 and 1 mg/kg, 0.0001 mg/kg and 0.75 mg/kg, 0.0001 mg/kg and 0.5 mg/kg, 0.0001 mg/kg to 0.25 mg/kg, 0.0001 to 0.15 mg/kg, 0.0001 to 0.10 mg/kg, 0.001 to 0.5 mg/kg, 0.01 to 0.25 mg/kg or 0.01 to 0.10 mg/kg of the patient's body weight. Generally, human antibodies have a longer half-life within the human body than antibodies from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human antibodies and less frequent administration is often possible. Further, the dosage and frequency of administration of antibodies of the invention or fragments thereof may be reduced by enhancing uptake and tissue penetration of the antibodies by modifications such as, for example, lipidation.

The therapeutics of the present invention may also be administered by controlled release means or delivery devices that are well known to those of ordinary skill in the art, such as those described in U.S. Patent Nos. 3,845,770; 3,916,899; 3,536,809; 3,598,123; and 4,008,719, 5,674,533, 5,059,595, 5,591,767, 5,120,548, 5,073,543, 5,639,476, 5,354,556, and 5,733,566. These controlled release compositions can be used to provide slow or controlled-release of one or more of the active ingredients therein using, for example, hydropropylmethyl cellulose, other polymer matrices, gels, permeable membranes, osmotic systems, multilayer coatings, microparticles, liposomes, microspheres, or the like, or a combination thereof to provide the desired release profile in varying proportions. Suitable controlled-release formulations known to those of ordinary skill in the art may be readily selected for use with the pharmaceutical compositions of the invention.

Controlled-release pharmaceutical products have a common goal of improving drug therapy over that achieved by their non-controlled counterparts. Ideally, the use of an optimally designed controlled-release preparation in medical treatment is characterized by a minimum of drug substance being employed to cure or control the condition in a minimum amount of time. Advantages of controlled-release formulations may include extended activity of the drug, reduced dosage frequency, and/or increased patient compliance.

Most controlled-release formulations are designed to initially release an amount of the therapeutic that promptly produces the desired therapeutic effect, and gradually and continually releases other amounts of the therapeutic to maintain the appropriate level of therapeutic effect over an extended period of time. In order to maintain this constant level of therapeutic in the body, the therapeutic must be released from the composition at a rate that will replace the amount of therapeutic being metabolized and excreted from the body. The controlled-release of the therapeutic may be stimulated by various inducers, for example, pH, temperature, enzymes, water, or other physiological conditions or compounds. Such controlled-release components in the context of the present invention include, but are not limited to, polymers, polymer matrices, gels, permeable membranes, liposomes, microspheres, or the like, or a combination thereof, that facilitates the controlled-release of the active ingredient.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or

biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

A therapeutic agent can be co-administering with one or more of a chemotherapeutic agent, a biomarker ligand, RAR selective ligand, radiation agent, hormonal agent (e.g., megestrol acetate), biological agent (e.g., stem cell, antibody) or an anti-inflammatory agent to the subject. Chemotherapeutic agents may be one or more of tamoxifen, trastuzumab (herceptin), raloxifene, doxorubicin, fluorouracil/5-flu, pamidronate disodium, anastrozole, exemestane, cyclophosphamide, epirubicin, letrozole, toremifene, fulvestrant, fluoxymesterone, trastuzumab, methotrexate, megestrol acetate, docetaxel, paclitaxel, testolactone, aziridine, vinblastine, capecitabine, goselerin acetate, zoledronic acid, and/or taxol.

Compounds that may be co-administered with therapeutic agents include steroid or a non-steroidal anti-inflammatory agent. Useful non-steroidal anti-inflammatory agents, include, but are not limited to, aspirin, ibuprofen, diclofenac, naproxen, benoxaprofen, flurbiprofen, fenoprofen, flubufen, ketoprofen, indoprofen, piroprofen, carprofen, oxaprozin, pramoprofen, muprofen, trioxaprofen, suprofen, aminoprofen, tiaprofenic acid, fluprofen, bucloxic acid, indomethacin, sulindac, tolmetin, zomepirac, tiopinac, zidometacin, acetaminophen, fentiazac, clidanan, oxipinac, mefenamic acid, meclofenamic acid, flufenamic acid, niflumic acid, tolfenamic acid, diflunisal, flufenisal, piroxicam, sudoxicam, isoxicam; salicylic acid derivatives, including aspirin, sodium salicylate, choline magnesium trisalicylate, salsalate, diflunisal, salicylsalicylic acid, sulfasalazine, and olsalazin; para-aminophenol derivatives including acetaminophen and phenacetin; indole and indene acetic acids, including indomethacin, sulindac, and etodolac; heteroaryl acetic acids, including tolmetin, diclofenac, and ketorolac; anthranilic acids (fenamates), including mefenamic acid, and meclofenamic acid; enolic acids, including oxicams (piroxicam, tenoxicam), and pyrazolidinediones (phenylbutazone, oxyphenbutazone); and alkanones, including nabumetone and pharmaceutically acceptable salts thereof and mixtures thereof. For a more detailed description of the NSAIDs, see Paul A. Insel, *Analgesic-Antipyretic and Antiinflammatory Agents and Drugs Employed in the Treatment of Gout*, in Goodman & Gilman's *The Pharmacological Basis of therapeutics* 617-57 (Perry B. Molinoff and Raymond W. Ruddon eds., 9<sup>th</sup> ed 1996) and Glen R. Hanson, *Analgesic, Antipyretic and Anti-Inflammatory Drugs in Remington: The Science and Practice of Pharmacy Vol II* 1196-1221 (A.R. Gennaro ed. 19<sup>th</sup> ed. 1995) which are hereby incorporated by reference in their entireties.

Other examples of agents that may be co-administered include, but are not limited to, immunomodulatory agents, anti-inflammatory agents (e.g., adrenocorticoids, corticosteroids

(e.g., beclomethasone, budesonide, flunisolide, fluticasone, triamcinolone, methylprednisolone, prednisolone, prednisone, hydrocortisone), glucocorticoids, steroids, non-steroidal anti-inflammatory drugs (e.g., aspirin, ibuprofen, diclofenac, and COX-2 inhibitors), and leukotriene antagonists (e.g., montelukast, methyl xanthines, zafirlukast, and zileuton),  
5 beta2-agonists (e.g., albuterol, biterol, fenoterol, isoetharine, metaproterenol, pirbuterol, salbutamol, terbutaline, formoterol, salmeterol, and salbutamol terbutaline), anticholinergic agents (e.g., ipratropium bromide and oxitropium bromide), sulphasalazine, penicillamine, dapsone, antihistamines, anti-malarial agents (e.g., hydroxychloroquine), anti-viral agents, and antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, erythromycin, penicillin,  
10 mithramycin, and anthracycline (AMC)).

Other compounds that may be co-administered with an a biomarker directed therapy include, anti-bacterial, anti-fungal, anti-viral, anti-hypertension, anti-depression, anti-anxiety, and anti-arthritis substances, as well as substances for the treatment of allergies, diabetes, hypercholesterolemia, osteoporosis, Alzheimer's disease, Parkinson's disease, and/or other  
15 neurodegenerative diseases, and obesity. Specific categories of test substances can include, but are not limited to, PPAR agonists, HIV protease inhibitors, anti-inflammatory drugs, estrogenic drugs, anti-estrogenic drugs, antihistamines, muscle relaxants, anti-anxiety drugs, anti-psychotic drugs, and anti-angina drugs. Other drugs may be co-administered with a biomarker related therapies according to the needs of a particular subject.

20 Suitable dosages are well known in the art. See, e.g., Wells *et al.*, eds., Pharmacotherapy Handbook, 2nd Edition, Appleton and Lange, Stamford, Conn. (2000); PDR Pharmacopoeia, Tarascon Pocket Pharmacopoeia 2000, Deluxe Edition, Tarascon Publishing, Loma Linda, Calif. (2000), each of which references are entirely incorporated herein by reference.

25 The foregoing and other useful combination therapies will be understood and appreciated by those of skill in the art. Potential advantages of such combination therapies include the ability to use less of each of the individual active ingredients to minimize toxic side effects, synergistic improvements in efficacy, improved ease of administration or use and/or reduced overall expense of compound preparation or formulation. The biological  
30 activities of a compound of this invention can be evaluated by a number of cell-based assays.

In combination therapy treatment, both the compounds of this invention and the other drug agent(s) are administered to mammals (e.g., humans, male or female) by conventional methods. The agents may be administered in a single dosage form or in separate dosage forms. Effective amounts of the other therapeutic agents are well known to those skilled in

the art. However, it is well within the skilled artisan's purview to determine the other therapeutic agent's optimal effective-amount range. In one embodiment of the invention where another therapeutic agent is administered to an animal, the effective amount of the compound of this invention is less than its effective amount would be where the other  
5 therapeutic agent is not administered. In another embodiment, the effective amount of the conventional agent is less than its effective amount would be where the compound of this invention is not administered. In this way, undesired side effects associated with high doses of either agent may be minimized. Other potential advantages (including without limitation improved dosing regimens and/or reduced drug cost) will be apparent to those of skill in the  
10 art.

In various embodiments, the therapies (*e.g.*, prophylactic and/or therapeutic agents) are administered less than 5 minutes apart, less than 30 minutes apart, 1 hour apart, at about 1 hour apart, at about 1 to about 2 hours apart, at about 2 hours to about 3 hours apart, at about 3 hours to about 4 hours apart, at about 4 hours to about 5 hours apart, at about 5 hours to about  
15 6 hours apart, at about 6 hours to about 7 hours apart, at about 7 hours to about 8 hours apart, at about 8 hours to about 9 hours apart, at about 9 hours to about 10 hours apart, at about 10 hours to about 11 hours apart, at about 11 hours to about 12 hours apart, at about 12 hours to 18 hours apart, 18 hours to 24 hours apart, 24 hours to 36 hours apart, 36 hours to 48 hours apart, 48 hours to 52 hours apart, 52 hours to 60 hours apart, 60 hours to 72 hours apart, 72  
20 hours to 84 hours apart, 84 hours to 96 hours apart, or 96 hours to 120 hours apart. In preferred embodiments, two or more therapies are administered within the same patent visit.

In certain embodiments, one or more compounds of the invention and one or more other therapies (*e.g.*, prophylactic or therapeutic agents) are cyclically administered. Cycling therapy involves the administration of a first therapy (*e.g.*, a first prophylactic or therapeutic agent) for a period of time, followed by the administration of a second therapy (*e.g.*, a second  
25 prophylactic or therapeutic agent) for a period of time, optionally, followed by the administration of a third therapy (*e.g.*, prophylactic or therapeutic agent) for a period of time and so forth, and repeating this sequential administration, *i.e.*, the cycle in order to reduce the development of resistance to one of the therapies, to avoid or reduce the side effects of one of  
30 the therapies, and/or to improve the efficacy of the therapies.

In certain embodiments, the administration of the same compounds of the invention may be repeated and the administrations may be separated by at least 1 day, 2 days, 3 days, 5 days, 10 days, 15 days, 30 days, 45 days, 2 months, 75 days, 3 months, or at least 6 months. In other embodiments, the administration of the same therapy (*e.g.*, prophylactic or



therapeutic agent) other than a compound of the invention may be repeated and the administration may be separated by at least at least 1 day, 2 days, 3 days, 5 days, 10 days, 15 days, 30 days, 45 days, 2 months, 75 days, 3 months, or at least 6 months.

Formulations and methods of administration that can be employed when the

- 5 Therapeutic comprises a modulating compound identified by the assays described, *supra*; additional appropriate formulations and routes of administration can be selected from among those described herein below. Moreover, a Therapeutic of the invention can be also be administered in conjunction with any known drug to treat the disease or disorder of the invention.
- 0 The gene product and/or the nucleic acid of discordantly expressed genes are potential drug candidates. For example, a gene product that is expressed in normal tissue, but not in injured tissue is a particularly attractive drug candidate that may be screened with the methods described herein.

#### KITS

- 15 In yet another aspect, the present invention provides kits for qualifying renal status, wherein the kits can be used to measure the markers of the present invention. For example, the kits can be used to measure any one or more of the markers described herein, which markers are differentially present in samples of renal cancer patient, ischemically injured subjects, and normal subjects. The kits of the invention have many applications. For
- 20 example, the kits can be used to differentiate if a subject has renal cancer or has a negative diagnosis, thus enabling the physician or clinician to diagnose the presence or absence of the cancer. The kits can also be used to monitor the patient's response to a course of treatment, enabling the physician to modify the treatment based upon the results of the test. In another example, the kits can be used to identify compounds that modulate expression of one or more
- 25 of the markers in *in vitro* or *in vivo* animal models for renal cancer.

- The present invention therefore provides kits comprising (a) a capture reagent that binds a biomarker selected from Table 9; and (b) a container comprising at least one of the biomarkers. In preferred kit, the capture reagent binds a plurality of the biomarkers. In certain preferred embodiments, the kit of further comprises a second capture reagent that binds
- 30 one of the biomarkers that the first capture reagent does not bind.

Further kits provided by the invention comprise (a) a first capture reagent that binds at least one biomarker selected from those listed in Table 9, and (b) a second capture reagent that

binds at least one of the biomarkers that is not bound by the first capture reagent. Preferably, at least one of the capture reagents is a nucleic acid.

While the capture reagent can be any type of reagent, preferably the reagent is a complementary nucleic acid probe.

5       The invention also provides kits comprising (a) a first capture reagent that binds at least one biomarker selected from Table 9, and (b) instructions for using the capture reagent to measure the biomarker. In certain of these kits, the capture reagent comprises a complementary nucleic acid probe. One embodiment of the present invention includes a high-throughput test for early detection of renal cancer, which analyzes a patient's sample on the  
10       nucleic acid chip array.

In other embodiments, the kits as described herein comprise at least one capture reagent that binds at least one biomarker selected from the markers listed in Table 9 and/or the markers of clusters 1 – 27.

15       Certain kits of the present invention further comprise a wash solution, or eluant, that selectively allows retention of the bound biomarker to the capture reagent as compared with other biomarkers after washing. Alternatively, the kit may contain instructions for making a wash solution, wherein the combination of the adsorbent and the wash solution allows detection of the markers using gas phase ion spectrometry.

20       Preferably, the kit comprises written instructions for use of the kit for detection of cancer and the instructions provide for contacting a test sample with the capture reagent and detecting one or more biomarkers retained by the capture reagent. For example, the kit may have standard instructions informing a consumer how to wash the capture reagent (e.g., probe) after a sample of blood serum contacts the capture reagent. In another example, the kit may have instructions for pre-fractionating a sample to reduce complexity of proteins in the  
25       sample. In another example, the kit may have instructions for automating the fractionation or other processes.

Such kits can be prepared from the materials described above, and the previous discussion of these materials (e.g., probe substrates, capture reagents, adsorbents, washing solutions, *etc.*) is fully applicable to this section and will not be repeated.

30       In another embodiment, a kit comprises (a) an antibody that specifically binds to a marker; and (b) a detection reagent. Such kits can be prepared from the materials described above, and the previous discussion regarding the materials (e.g., antibodies, detection reagents, immobilized supports, *etc.*) is fully applicable to this section and will not be

repeated. Optionally, the kit may further comprise pre-fractionation spin columns. In some embodiments, the kit may further comprise instructions for suitable operation parameters in the form of a label or a separate insert.

Optionally, the kit may further comprise a standard or control information so that the test sample can be compared with the control information standard to determine if the test amount of a marker detected in a sample is a diagnostic amount consistent with a diagnosis of renal cancer.

The present invention also provides a screening assay comprising (a) contacting a cancer cell with a test agent and (b) determining whether the test agent modulates the activity of any one or more of the biomarkers listed in Table 9. The biomarkers of Table 9 include any of the discordantly or concordantly expressed genes between the RRR and RCC models and normal cells. The examples below and Tables show numerous examples of biomarkers that are useful for screening assays.

Kits, according to the invention, may include reagents, including primers, polymerases, antibodies, buffers, nucleic acid chips, protein chips, antibody chips and/or labels. The kit may also include, microscope slides, reaction vessels, instruction for use of the reagents and material and how to interpret the data generated from the assays. For example, PCR primers for the amplification of the a biomarker transcript may also be included. Antibodies to detect the a biomarker proteins may also be included in the kit.

## EXAMPLES

It should be appreciated that the invention should not be construed to be limited to the examples which are now described; rather, the invention should be construed to include any and all applications provided herein and all equivalent variations within the skill of the ordinary artisan.

### EXAMPLE 1

Using gene expression profiling, we investigated in a rodent model the gene expression changes relative to normal kidney, occurring after ischemia/reperfusion injury and during the first two weeks of RRR. Consequently, a detailed analysis revealed distinct regenerative gene expression patterns, pathways, transcriptional control and gene functions. The RRR differential gene expression was then qualitatively compared with the global gene expression of RCC as opposed to human normal kidney. Two distinct signatures were

revealed: (1) a substantial concordant overlap reflecting the normal regenerative phenotype, and (2) a divergent discordant (inverted) pattern of expression where gene expression changes are in opposite direction in RRR and RCC.

### **Animals**

The mice were 5-week-old C57BL/6 female mice (60 to 100 g) and obtained from the National Institute of Health (NIH). The animals had free access to water and food. Animal care and experiments were performed with the approval of the Animal Care and Use Committee of the National Cancer Institute, Maryland.

### **Ischemia-reperfusion model**

Regeneration was induced by the renal warm ischemia method (Chiao H 1997, Chiao H 1998). Mice were anesthetized with ketamine, xylazine, and acepromazine and placed on a heating table kept at 37°C to maintain constant body temperature. A left unilateral flank incision was made, the left kidney perirenal fat removed, and the left renal artery exposed. A non-traumatic vascular clamp was placed across the renal artery for 50 minutes. After removal of the clamp, the kidney was inspected for restoration of blood flow, and 1 ml of pre-warmed (37°C) normal saline was instilled into the abdominal cavity. The abdomen was closed with wound clips (Roboz Surgical Instrument Co., Inc, RS-9262), and the animals were allowed to recover in a 37°C incubator. After the desired period of reperfusion (0, 6, and 12 hours and on days 1, 2, 5, 7 and 14), the animals were anesthetized and both kidneys were rapidly excised by midline abdominal incision. For microarray studies, the kidneys were flash frozen in liquid nitrogen and stored at -70°C. For histological studies, the kidneys were bivalved with a coronal cut and fixed in formalin (10%). Normal and ischemic kidneys were removed, processed, and frozen in an identical manner.

### **Immunohistochemistry**

Fixed and paraffin-embedded tissue specimens were deparaffinized, rehydrated, subjected antigen unmasking (Morgan JM et al 1994), and treated to nonspecific block staining. For this latter procedure, sections were incubated for 20 min at 24 °C with 1% H<sub>2</sub>O<sub>2</sub> in methanol, followed by blocking for 30 min with 5% normal horse serum in PBS. Polyclonal antibodies against Ki67 (NOVO, NCL-Ki67p) or mouse glucose transporter (Glut-1) (Alpha Diagnostic Intl; GT11-A) were added (1:1000 dilution) for 16 h at 4 °C, followed by incubation for 30 min at room temperature with biotinylated secondary goat anti-rabbit IgG antibodies and 30 min with avidin-biotin peroxidase conjugate (1:50 dilution) (Vectastain Elite Universal kit: Vector Laboratories, Burlingame, California). Color was developed using Vector Labs 3,3-Diaminobenzidine kit for 10 min followed by counterstaining with Mayer's

hematoxylin. Negative controls were performed using nonimmune serum or PBS. Three investigators independently evaluated the immunohistochemistry.

### Microarray procedures

Mouse cDNA microarrays (NIH/NCI GEM2) containing 9646 cDNA spots were used to quantitate mRNA expression in the kidney samples. A reference probe consisting of an equal mixture of 6 normal mouse tissues (brain, heart, kidney, liver, lung and spleen) was used in the competitive hybridization experiments. For the reference probe 50 ug of total RNA were reverse transcribed, and to avoid an amplification step for the experimental sample, 3.0 ug of poly(A)<sup>+</sup> RNA were subjected to oligo(dT)-primed reverse transcription. The remaining procedures were performed as described previously (Rosenwald et al., 2002). See Table 9.

### Quantitative Real-Time RT-PCR

RNA was isolated using Trizol Reagent (Invitrogen, California). Total RNA (1 g) was reverse transcribed in a volume of 50  $\mu$ l. 5  $\mu$ l of the resulting solution was then used for PCR according to the manufacturer's instructions (Applied Biosystems, Foster City, CA). Gene expression for *IGFBP1*, *IGFBP3*, *CTGF*, *AKT*, *FRAP*, *MYC*, *NF- $\kappa$ B*, *HK1* and *SIRT7* were quantified relative to the expression level of ribosomal 18s. *PHD1*, *PHD2* and *PHD3* were quantified relative to the expression level of filamin B, (actin binding protein 278; FLNB). All probes were purchased from Applied Biosystems, Inc. (Foster City, CA). Normalized data are presented as -fold difference in  $\log_2$  gene expression.

### Motif selection

Statistical analysis of transcription factor binding sites in the current set of up- and down-regulated genes. We retrieved 1-kb sequences in the upstream region of the genes for 523 up- and 318 down-regulated genes (a subset of 1325 up/down genes). The 1-kb sequences in the promoter regions were used to search for transcription factor (TF) binding sites using a TransFac web server. To identify TF binding sites enriched in the set of up- or down-regulated genes, we used Fisher's exact test to search TF sites that differed significantly between the up- and down-regulated genes. We constructed a 2X2 table with up/down genes and presence/absence of TF sites for each of the 177 TF sites (see Method). Four p-value cutoffs were used to select up/down genes and fisher's test was used to test each table.

### Analysis Of Currated Pathway Genes

Using PubMed, a survey of the literature published from 1966 through mid 2003 was performed, and differentially expressed genes in the following categories were extensively

catalogued: RCC vs. normal kidney; renal cell culture hypoxia responsive genes vs. normoxia-responsive genes; HIF-regulated genes; VHL, IGF, MYC, NF- $\kappa$ B pathway genes; purine pathway genes; genes expressed following renal ischemia reperfusion and/or ARF vs. genes expressed in normal kidney; and the tissue expression pattern of renal genes (e-renal histology). The gene datasets were translated into a distinct set of gene identifiers (i.e., the HUGO gene symbol) that were used to facilitate cross comparisons among datasets. Only genes that were printed on the GEM2 microarray were considered for further analysis (differentially expressed and unchanged expression).

To navigate among gene identifiers, the programs MatchMiner (<http://discover.nci.nih.gov/matchminer/html/index.jsp>) and SOURCE (<http://source.stanford.edu>) were used.

The enrichment of genes in various pathways in concordant or discordant groups was analyzed by using the chi square test (tables 3, 4 and 12). An example of 2X2 contingency table is shown immediately below:

	Concord	Remainder
Hypoxia pathway	35	216
Remainder	243	5302

251 genes were mapped to the hypoxia pathway and printed on the GEM2 array, 35 of which showed concordant expression with a remainder of 216 in the first row. A total of 278 genes are located in the first column, 35 of which showed concordant expression with a remainder of 243. 5,796 genes were on the microarray, producing a remainder of 5302 genes in column 2 (5796-35-216-243). The p-value for the 2X2 table was calculated using Statistic Package R.

In order to establish an understanding of the process of renal regeneration repair (RRR) and its relationship to the gene expression changes in renal cell carcinoma (RCC), we first characterized histopathological changes and differential gene expression as a consequence of 50 minutes warm ischemia in a murine model of renal RRR (Fig. 1), (Suparvekin S. et al 2003). We then compared the gene expression patterns, pathways, transcriptional control and gene functions of RRR to RCC. To accomplish this study, the following five steps were performed and are described below: (1) characterization of the process of RRR by temporal histopathology changes; (2) characterization of the differential gene expression as a consequence of RRR; (3) Identification of specific functional gene-clusters by ontology analysis, probabilistic functional genomics and cross-comparison with the pathway literature; (4) identification of similarities and differences in gene expression between RRR and RCC;

(5) analysis of biological meaning of concordant and discordant genes associated with RRR and RCC.

### Characterization of the histopathology of RRR

Early histopathologic features of ischemic injury induced by 50 minutes of vascular clump were readily evident in the kidney within the first 12 hours of reperfusion and were monitored at 1, 2, 5, 7 and 14 days. As expected, we observed apoptotic cells in the outer medulla within 12 hours of reperfusion, which became more abundant over the first 24 hours following initial injury (Suparvekin S. et al 2003) (data not shown). At one day after the ischemic event, more than half of cortical tubules (Fig. 2C) showed some degree of staining for glucose transporter-1 (Glut-1/ SLC2A1), which is regulated by the transcription factor hypoxia-inducible factor 1 (HIF1). Up-regulation of HIF1 provides tissue protection from ischemic damage during the early regeneration phase (Matsumoto M. et al 2003). At 2 days, we observed by hematoxylin and eosin (H&E) staining an acute tubular necrosis in which about half of the tubules showed necrosis with loss of epithelium; the remaining tubules showed cells with reactive nuclear changes (hyperchromasia, prominent nucleoli) (Fig. 2A, 2B). At 2 days, the necrotic-apoptotic events were accompanied by positive tubules staining with the proliferation marker MiB-1 (Fig. 2B). At two weeks, most tubules showed a normal appearance with only rare examples showing degenerative or regenerative changes (Fig. 2B). Thus, the histological evidence reported here supports the accepted process of renal injury, regeneration, and recovery (Sutton TA et al 2002). Damaged renal tissue is first characterized by regenerating tubules in which necrotic cells are accompanied by replicating cells; at two weeks, most tubules have recovered and regained their normal appearance.

### Characterization of differential gene expression as a consequence of renal IRI: Defined phases of early, late and continuous tissue regeneration

Employing cDNA microarray analysis of 9,646 genes, we were able to compare the changes in the global pattern of gene expression of normal (day 0), ischemic (50 minutes) and reperused (at 1, 2, 5 and 14 days) kidney tissue. A differential expression pattern was observed for a group of 1,350 gene spots, corresponding to 1,325 genes ( $P$ -value  $\leq 0.05$ ). This differential pattern clustered into a dendrogram consisting of four main branches (Fig. 3, 1s). The first branch included the normal and ischemic kidney tissue; the second branch included genes accompanying regenerative processes taking place continuously throughout the two-week period (Fig. 3 marked as asterisk); the third branch was of genes expressed during early regenerative processes taking place during the first two days following reperfusion (Fig. 3

marked as A); and finally, the fourth branch included genes expressed late, at 5 and 14 days after reperfusion (Fig. 3 marked as B).

The differential expression of each gene was averaged and calculated as relative to the same gene expressed in normal and ischemic kidney tissues. All the repetitive samples clustered together, illustrating the reproducibility of the animal model and supporting the reliability of the array methodologies employed. Therefore, relative to the normal kidney, we identified three phases of RRR: continuous, early and late.

Of the 1,325 RRR genes that were differentially expressed from normal kidney during the first two weeks, 323 genes were continuously differentially expressed throughout the period (189 up-regulated and 134 genes down-regulated); in the early phase of RRR, 629 were differentially expressed (336 up-regulated and 293 down-regulated) and in the late phase of RRR, 373 genes were differentially expressed (227 were up-regulated and 96 down-regulated), (Table 1). Table 1 summarizes the data related to the amount of genes that were differentially expressed and are therefore of potential functional importance in general biological processes involved in RRR. A complete listing of all genes is given in Table 9.

The RRR differential gene expression as opposed to normal kidney was further clustered to identify different temporal patterns/ trends. We statistically identified 27 trends. Trend 1 (Fig. 4A) represents the major patterns of genes that were down-regulated during RRR and partially returned towards normal levels, by day 14, (n=270). Trend 2 or 4 (Fig. 4B) is the pattern seen for 199 genes that were up-regulated at the early phase (days 1 and 2) and reduced towards normal levels at the late phase (days 5 and 14). Trend 5 (Fig. 4C) represents 190 genes that were early up-regulated and remained up-regulated on the 14th day of RRR. Trend 16 (Fig. 4D) contains 87 genes that were down-regulated at days 1 and 2, but were back to normal levels on day 5. Other patterns are discerned statistically, but follow similar tendency as the representative trends shown, which contain the majority of the differentially expressed genes.

#### **Identification of specific functional gene-clusters by ontology analysis, probabilistic functional genomics, and cross-comparison with the pathway literature**

The gene expression of RRR phases according to biological processes, molecular functions, and cellular expression patterns by gene ontology (<http://www.geneontology.org>) was analyzed. The analysis is summarized in Table 10.

During the early phase, the unique ontologies with a majority of up-regulated genes were either DNA replication or entrance into the S-phase of the mitotic cell cycle. Ontologies of a majority of early phase, down-regulated genes were oxidative phosphorylation,



metabolism, growth factor binding and. Both up- and down-regulated early phase genes were regulators of translation, cell growth, and/or cell maintenance—all processes that are required for cell survival and growth (Table 10).

During the late phase, after tissue regeneration began, the biological processes associated with a majority of up-regulated genes were related to inflammation and catabolism at the proteasome core complex, microfibril and the ECM. These late, up-regulated genes modulated several distinct molecular functions—MHC class I receptor activity, collagenase activity, phospholipase inhibitor activity, hydrolase activity-actions on carbon-nitrogen (but not peptide) bonds, apoptosis inhibitor activity, peptidase activity, and receptor activity.

Biological processes associated with both late up- and down -regulated genes were mainly urea cycle intermediate metabolism and the response to wounding (Table 10).

Throughout the entire RRR process, ontologies with a majority of continuously up-regulated genes were of ribosome biogenesis and assembly; protein biosynthesis; cytoplasm organization; biogenesis; and biological responses to abiotic (non-living) stimulus.

Continuously up-regulated genes were associated with molecular functions that included immunoglobulin binding, chemokine activity, G-protein-coupled receptor binding actin binding, RNA binding, and finally, processes accompanying the defense response following injury, which are also significant during the late phase of RRR. The ontologies associated with a majority of continuously down-regulated genes were related to the processes of phenylalanine metabolism and catabolism as well as fatty acid metabolism, which was also significant during the early phase of RRR. The continuously down-regulated genes were associated with the function of anion transporter activity; and oxidoreductase activity, the latter of which is also significant during the early phase. The continuously phase ontologies with both up- and down-regulated genes were of inorganic anion transport; posttranslational membrane biomarkering, blood coagulation, endoplasmic reticulum (ER) organization, and biogenesis. The cellular components that were affected during the continuous phase included the cytosolic ribosome, the actin filament, the ECM and the mitochondrion (Table 2, 3-supplement).

To further understand the relationships from the current 1325 RRR differentially expressed genes with the literature databases and genome-wide promoter analysis, we reviewed the evidence reported in the literature on the pathways and regulators previously described in both RRR and RCC. The pathways of focus for detailed analysis were in respect to the VHL tumor suppressor, and included hypoxia, interacting proteins and biomarker genes of VHL, HIFs (HRE), Myc, p53, NF-kB and IGF (Elson D.A. et al., 2000, Maxwell PH. 2004,

Schips L et al 2004, Hammerman MR 1999, Yamaguchi S et al 2003, Koshiji M et al 2004, Schmid T et al 2004, Qi H and Ohh M 2004, Cao CC et al 2004). The VHL pathway database included 865 genes of which 341 genes were printed on the GEM2 array and 104 genes were differentially expressed. The VHL database included interacting proteins and genes that

5 differentially expressed dependently of the VHL in renal cells and dependent or not on oxygen (Table 9). The database of the hypoxia regulated genes included 551 genes regulated by hypoxia of which 251 genes were printed on the GEM2 array and 95 genes were differentially expressed. Of the hypoxia regulated genes in our database, the promoter of 45 genes included an HRE, 39 were printed on the array and of which 17 were differentially regulated (Table 9).

10 The Myc pathway included 728 genes including biomarker gene and interacting proteins. 368 genes of the Myc pathway database were printed on the GEM2 array of which 136 were differentially expressed (Table 9). The p53 pathway dataset included 2,808 genes including p53 biomarker genes of cell adhesion, cell cycle, miscellaneous, structural, tumor suppressor/apoptosis, GDT/GTP binding, growth factors and hormone, lymphocyte signaling,

15 Membrane receptor, neurobiology, protein kinase, protein phosphatase, steroid receptor and transcription regulation (Hoh J et al (2002)), (Table 9). 1259 genes of the p53 pathway database were printed on the GEM2 array and of which 262 were differentially expressed. The NF- $\kappa$ B pathway database included 446 genes that included biomarker genes, inducers, interacting proteins and inhibitors. 200 of these genes were printed on the GEM2 array and of

20 which 52 genes were differentially expressed (Table 9). The IGF pathway database included 306 genes as biomarker genes, inducers, interacting proteins and inhibitors of which 139 genes were printed on the GEM2 array and 52 were differentially expressed (Table 9).

The comparison of the 1325 RRR differentially expressed genes with genes in these pathways was significantly ( $p < 0.05$ ) associated with the pathways of VHL, hypoxia, HIF1a (HRE) and Myc. Biomarker genes and regulators in the pathways of IGF, p53 and NF- $\kappa$ B  
25 were also evident, but with association significance of  $p > 0.05$  for the whole 1325 RRR differentially expressed genes (Table 4).

We next compared the up-regulated (189 genes) and down-regulated (134 genes) genes of the current RRR dataset with the genes in the pathways associated with VHL gene.

30 Genes in both sub-sets played significant roles ( $p < 0.05$ ) as components of pathways associated with VHL, Myc, p53 and NF- $\kappa$ B. As subsets of the 1,325 genes, the up- or down-regulated genes were evident, but with association significance of  $p > 0.05$ , for pathways associated with Hypoxia, or HIF (HRE) (Table 4, 1-supplement).

#### Similarities and differences between RRR and RCC

We next investigated similarities and differences between gene expression associated with RRR and those reported to be associated with RCC. We extensively surveyed the literature and cataloged 984 genes expressed differentially in RCC as relative to normal kidney (Table 1- supplement) (Riss et al., 2004 review in preparation). Then RCC dataset was qualitatively cross-compared with the differential expression of the current set of 1,325 RRR genes as relative to normal kidney.

The analysis revealed a group of 361 genes that matched both the experimental RRR dataset and the RCC literature (Fig 4A, Table 9). Of these 361 genes, 285 genes (77%) were concordantly expressed in both RRR and in RCC; 209 genes were up-regulated (i.e. VCAM1, ICAM1, MYC, MMP14, MDM2, STAT3, ID2, TIMP1, CD44, ITGB1 and AKT1), (P<0.001), while 69 genes were down-regulated (P<0.001) both in RRR and in RCC (i.e. EGF, JUP, SDHB, SLC12A1, and CALB1), (Fig 4B, Table 9).

Previous reports suggested that RRR and or RCC subject to regulation by hypoxia and a number of pathways as VHL, HIF, IGF, Myc, p53 and NF-kB (Elson D.A. et al., 2000, Maxwell PH. 2004, Schips L et al 2004, Hammerman MR 1999, Yamaguchi S et al 2003, Koshiji M et al 2004, Schmid T et al 2004, Qi H and Ohh M 2004, Cao CC et al 2004). We therefore tested if biomarker genes of these pathways or their regulators were significantly found in the 285 concordantly expressed genes. In both RRR and RCC the concordant genes significantly (p<0.05) included genes regulated by hypoxia and pathways as VHL, Myc, p53 and NF-kB. HIF and IGF pathway genes were also evident among the concordant genes but with association significance of p>0.05.

The concordant genes were significantly (p<0.05) expressed in six of the temporal patterns/ trends of gene expression and included the up-regulated trends: 2, 4, 6, 14 and the down-regulated trends 1 and 16 (Table 6- supplement; Fig 5). Further, trends 1, 4, 6 and 14 were significant to the concordant genes and not to the discordant one (the temporal patterns/ trends of gene expression are described in the Characterization of differential gene expression as a consequence of renal Ischemia) (Table 6-supplement).

The remainder of the 361 genes, 83 genes (23%), were discordantly expressed during RRR as compared to RCC. Of these 83 discordant genes, 30 genes were in RRR up-regulated and in RCC down-regulated (P<0.001). The remaining 53 genes were down-regulated in RRR and up-regulated in RCC (P<0.001). Of significance (p<0.05) were genes in the pathways of VHL, hypoxia, HIF1a (HRE), IGF, and p53. HIF and IGF pathways are significantly unique to the discordant genes and not for the concordant genes. On the other hand, genes in the NF-kB pathway were significant for the concordant genes, but only evident among the discordant

genes, with association significance of  $p > 0.05$ .

Three temporal patterns/ trends of gene expression, down-regulated trends 2, 11, and the up-regulated trend 16, significantly included discordant genes ( $p < 0.05$ ). Trend 11 was significantly unique to the discordant genes and not the concordant genes. Trend 11 trend encompassed 46 down-regulated genes (9 of which were discordantly expressed) active from the first day until the fifth day of RRR, when they began to return to normal levels of expression (Table 6- supplement; Fig 5).

Therefore the RRR shares with RCC two qualitative gene expression signatures: a concordant and a discordant. The genes in the two signatures are significantly subject to regulation by similar pathways as well as significantly unique pathways ( $p < 0.05$ ). The probability of being able to observe these concordant (77% RRR/ RCC) and discordant (23% RRR/ RCC) genes merely through chance would be extremely low if RRR and RCC phenotype were unrelated ( $p$ -value  $2.2e-16$ , binomial test).

#### **The Biological Basis Of Concordantly And Discordantly Expressed Genes In RRR And RCC**

In the search for the biological basis of the concordant and discordant groups, we analyzed these genes using the Gene Ontology consortium ontologies (GO), (Fisher Exact  $p < 0.05$ ), (<http://www.geneontology.org>). This method revealed that the concordant genes were significantly involved in such molecular functions as immunoglobulin binding, ECM structural constituent conferring tensile strength activity, structural constituents of ribosomes, RNA binding, cell adhesion (mainly by RRR up-regulated genes), and selenium binding (mainly by RRR down-regulated genes). The over all concordant gene expression was up-regulated in cellular components that included the cytosolic ribosome, the proteasome core complex, collagen, the small ribosomal subunit, and the microfibril. The biological processes with an overall concordant gene up-regulated expression were DNA replication initiation, ribosome biogenesis, macromolecule biosynthesis, cytoplasm organization and biogenesis, cell death, cell adhesion, immune response, and protein metabolism. Process with mainly down-regulated concordant genes included phenylalanine metabolism and catabolism, tyrosine metabolism, and cell ion homeostasis. Other significant processes affected included regulation of translation, posttranslational membrane biomarking, ER organization and biogenesis, and cell growth and/or maintenance (Table 6, 4-supplement).

On the other hand, the discordant genes were significantly (Fisher Exact  $p < 0.05$ ) found in molecular functions as insulin-like growth factor binding, organic cation transporter activity, and heparin binding. The discordant genes were significant in the cellular component

of extracellular space and were significantly associated with the molecular processes of one-carbon compound metabolism, angiogenesis, regulation of cell growth, actin cytoskeleton organization and biogenesis, actin filament-based processes, enzyme-linked receptor protein signaling, organelle organization and biogenesis, and organogenesis (Table 6, 4-supplement).

5        Following this analysis, we then cross-compared gene ontologies (Fisher Exact  $p < 0.05$ ), among the concordant group, the discordant group, and the group continuously involved in all three phases of RRR, which we correlated above with Sutton's four-phase model of RRR (Sutton TA et al 2002).

10        During the early phase of RRR the gene category of DNA replication initiation was significantly present and consisted of five up-regulated genes. These five genes belong to the family of minichromosome maintenance proteins (MCM) and included MCM2, MCM3, MCM4, MCM5, and MCM7. With the exception of MCM5, these genes have been reported to be up-regulated concordantly in RCC pathogenesis (Table 1-supplement, Table 6).

15        The discordant genes significantly shared the ontology of growth factor binding with the early phase, and the ontology of extracellular space with the late phase (Table 5-supplement). During the early phase, discordant genes in the "growth factor binding" ontology were associated with the IGF pathway. Both connective tissue growth factor (CTGF/IGFBP8) and cysteine-rich protein 61 (CYR61) were up-regulated in RRR, while insulin-like growth factor binding proteins 1 and 3 (IGFBP1 and 3) were down-regulated in  
20        RRR. The discordant genes belonging to the late phase ontology of extracellular space that were up-regulated in RRR and included apolipoprotein E (APOE), connective tissue growth factor (CTGF), decorin (DCN), glypican 3 (GPC3), matrix metalloproteinase 2 (MMP2), plasminogen activator, tissue (PLAT), and thrombospondin 1 (THBS1). In contrast, growth arrest and D-damage-inducible 45 gamma (GADD45G) was down-regulated in RRR. Except  
25        for GADD45G, the genes of this group shared a pattern of expression with trends 5 and 6, which were also up-regulated in RRR at two weeks after the initial trauma (Table 6).

30        Among its 46-gene complement, trend 11 contains 4 concordant ( $p > 0.05$ ) and 9 significant discordant genes ( $p < 0.0003$ ). All of these genes proved to be down-regulated in RRR and included superoxide dismutase 2 (SOD2), cytochrome c oxidase subunit VIc (COX6C), kinesin family member 21A (KIF21A), kallikrein 1 (KLK1), heat shock  
105kDa/110kDa protein 1 (HSPH1), carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1), methionine adenosyltransferase II, alpha (MAT2A), PCTAIRE protein kinase 3 (PCTK3), and serine hydroxymethyltransferase 2 (SHMT2). The last four genes were also regulated by the VHL pathway (Table 6).

We then extended the gene ontologies (Fisher Exact  $p < 0.05$ ) to a cross-comparison with the following groups: total gene-expression data, the sub-sets for early and/or late RRR, expression trends, pathways such as IGF, concordance and discordance with RCC, oncogenes, tumor suppressors, and metastasis (Figs. 4-supplement, 5, 6, 7).

The concordant genes and trend 2 (up-regulated in the early RRR and moderately down regulated at the late RRR) corresponded primarily with ontologies of ribosome and defense (Fig. 6). Possibly, a sub-set of this pattern was also involved in the Hypoxia and VHL pathways, senescence, and trend 4, which was up-regulated during early RRR, but returning to normal expression levels at two weeks of RRR (fig 6). P53 and NF-kB were regulating ontologies in defense/ immune responses, death process and ER genes (fig 6).

The ontologies involved in the IGF pathway were also present in the genes discordantly expressed between RCC and RRR. These included such processes as cell growth and angiogenesis and functions as growth factor binding, enzymatic reactions, glycosaminoglycan binding, and heparin binding. Finally, certain cellular components, including ECM, were co-represented in both the IGF pathway and the RCC discordant gene subset. Because both the IGF pathway and the discordant gene subset share genes to a significant degree, we suggest that the IGF pathway plays a functional role in RRR and RCC (Fig 5, 7).

We also catalogued the discordant genes on a non-probabilistic, gene-by-gene basis (Table 7). Most of the changed genes in the discordant group belong to subgroups that are important in maintaining cell structure, gene expression, ECM function, angiogenesis, DNA repair, catabolism, mitochondrial functions, motility, catalytic activity, stress signals, external signals, ubiquitination, immunity, oxidation, metastasis, migration, and adhesion. Similarly to the results of our previous analysis (Table 3), genes regulated discordantly when comparing normal RRR and RCC, proved or suggested to be regulated by the IGF, VHL-HIF, hypoxia, C-MYC, p53, or NF-kB pathways. Moreover, some of these genes are known to play roles in pathways involved in senescence, tumor suppression, or oncogenesis.

### Characterization of the histopathology of RRR

Early histopathologic features of ischemic injury induced by 50 minutes of vascular clump were readily evident in the kidney within the first 12 hours of reperfusion and were monitored at 1, 2, 5, 7 and 14 days. As expected (Suparvekin S. et al 2003), we observed apoptotic cells in the outer medulla within 12 hours of reperfusion, which became more abundant over the first 24 hours following initial injury (data not shown). At one day after the ischemic event, more than half of cortical tubules (Fig. 2C) showed some degree of staining

for glucose transporter-1 (Glut-1/ SLC2A1), which is regulated by the transcription factor hypoxia-inducible factor 1 (HIF1). Up-regulation of HIF1 provides tissue protection from ischemic damage during the early regeneration pattern (Matsumoto M. et al 2003). At 2 days, we observed by hematoxylin and eosin (H&E) staining an acute tubular necrosis in which about half of the tubules showed necrosis with loss of epithelium; the remaining tubules showed cells with reactive nuclear changes (hyperchromasia, prominent nucleoli) (Fig. 2A, 2B). At 2 days, the necrotic-apoptotic events were accompanied by positive tubules staining with the proliferation marker MiB-1 (Fig. 2B). At two weeks, most tubules showed a normal appearance with only rare examples showing degenerative or regenerative changes (Fig. 2B). Thus, the histological evidence reported here supports the accepted process of renal injury, regeneration, and recovery (Sutton TA et al 2002). Damaged renal tissue is first characterized by regenerating tubules in which necrotic cells are accompanied by replicating cells; at two weeks, most tubules have recovered and regained their normal appearance

#### **Characterization of differential gene expression as a consequence of renal RRR: Defined patterns of early, late and continuous tissue regeneration**

Employing cDNA microarray analysis of 9,646 genes, we were able to compare the changes in the global pattern of gene expression of normal (day 0), ischemic (50 minutes) and reperfused (at 1, 2, 5 and 14 days) kidney tissue. A differential expression pattern was observed for a group of 1,350 gene spots, corresponding to 1,325 genes ( $P$ -value  $\leq 0.05$ ). This differential pattern clustered into a dendrogram consisting of four main branches (Fig. 3, 9). The first branch included the normal and ischemic kidney tissue; the second branch included differentially expressed genes accompanying regenerative processes taking place continuously throughout the two-week period (Fig. 3 marked as asterisk); the third branch was of genes differentially expressed during early regenerative processes taking place during the first two days following reperfusion (Fig. 3 marked as A); and finally, the fourth branch included genes differentially expressed late, at 5 and 14 days after reperfusion (Fig. 3 marked as B).

The differential expression of each gene was averaged and calculated as relative to the same gene expressed in normal and ischemic kidney tissues. All the repetitive samples clustered together, illustrating the reproducibility of the animal model and supporting the reliability of the array methodologies employed. Therefore, relative to the normal kidney, we identified three patterns of differentially expressed genes during RRR: continuous, early and late.

Of the 1,325 RRR genes that were differentially expressed from normal kidney during the first two weeks, 323 genes were in the continuously pattern (189 genes up-regulated and

134 genes down-regulated); in the early pattern of RRR, 629 genes were differentially expressed (336 genes up-regulated and 293 genes down-regulated) and in the late pattern of RRR, 373 genes were differentially expressed (227 genes were up-regulated and 96 genes down-regulated), (Table 1). Table 1 summarizes the data related to the numbers of genes that were differentially expressed and are therefore of potential functional importance in general biological processes involved in RRR. A complete listing of all genes is given in the supplemented Table 9.

The RRR differential gene expression as compared to normal kidney was further clustered to identify different temporal trends over the two week period. We statistically identified 27 trends that are described in details in the supplemental material. The 6 major trends are represented in Fig. 4. The up-regulated trends (Fig. 4A-C) consists of trend 5 (Fig. 4A) that represents 190 genes that were early up-regulated and remained up-regulated on the 14<sup>th</sup> day of RRR and trends 2 and 4 (Fig. 4B-C) are of pattern seen for 194 and 37 genes, respectively, that were up-regulated at the early pattern (days 1 and 2) and reduced towards normal levels at the late pattern (days 5 and 14).

The down-regulated trends (Fig. 4D-E) consists of trend 1 (Fig. 4D) represents the major patterns of genes that were down-regulated during RRR and partially returned towards normal levels, by day 14, (n=270). Similarly, trends 16 and 11 (Fig. 4E, 4F) contain 87 and 11 genes, respectively, that were down-regulated at days 1 and 2, but were getting back to normal levels on day 5. Other temporal trends are discerned statistically, but follow similar tendency as the representative trends shown, which contain the majority of the differentially expressed genes.

#### **Identification of specific functional gene-clusters by ontology analysis, probabilistic functional genomics, and cross-comparison with the pathway literature**

##### **Similarities and differences between RRR and RCC**

Previous reports suggested that RRR and or RCC subject to regulation by hypoxia and a number of pathways as VHL, HIF, IGF, Myc, p53 and NF-kB (Elson D.A. et al., 2000, Maxwell PH. 2004, Schips L et al 2004, Hammerman MR 1999, Yamaguchi S et al 2003, Koshiji M et al 2004, Schmid T et al 2004, Qi H and Ohh M2004, Cao CC et al 2004). We therefore tested if biomarker genes of these pathways or their regulators were significantly found in the 285 concordantly expressed genes. In both RRR and RCC the concordant genes significantly ( $p < 0.05$ ) included genes regulated by hypoxia and pathways including VHL, Myc, p53 and NF-kB. HIF and IGF pathway genes were also evident among the concordant genes but with association significance of  $p > 0.05$  (Table 4).



The concordant genes were significantly ( $p < 0.05$ ) expressed in six of the temporal patterns/ trends of gene expression and included the up-regulated trends: 2, 4, 6, 14 and the down-regulated trends 1 and 16 (Fig 4 and supplemented Fig 10 and Table 12). Further, trends 1, 4, 6 and 14 were significant to the concordant genes and not to the discordant one (the temporal patterns/ trends of gene expression are described in the Characterization of differential gene expression as a consequence of renal Ischemia) (Fig 4 and supplemented Fig 10 and Table 12).

The remainder of the 361 genes, 81 genes (23%), were discordantly expressed during RRR as compared to RCC. Of these 83 discordant genes, 30 genes were in RRR up-regulated and in RCC down-regulated (i.e. FHIT, MMP2, APOE, CTGF, DCN, PLAT, THBS1, WSB1, SLC1A1, SMC1L1), (tables 7, 9). The rest of the 53 genes were down-regulated in RRR and up-regulated in RCC (i.e. IGFBP1, IGFBP1, PHD2/ EGLN1, Nulp1 (KIAA1049), VEGFA, KDR/VEGFR2, ACOX1, CPT1A, HK1, SLC16A7/ MCT2, RRM1, ENPP2, COX6C, TOP3B, PAPOLA/PAP and SLC22A1), (tables 7, 9). Of significance ( $p < 0.05$ ) were genes in the pathways of VHL, hypoxia, HIF1a (HRE), IGF, and p53. HIF and IGF pathways are significantly distinct to the discordant genes and not for the concordant genes. On the other hand, genes in the NF- $\kappa$ B pathway were significant for the concordant genes, but only evident among the discordant genes, with association significance of  $p > 0.05$  (Table 4).

Three temporal patterns/ trends of gene expression, down-regulated trends 2, 11, and the up-regulated trend 16, significantly included discordant genes ( $p < 0.05$ ). Trend 11 was significantly distinct to the discordant genes and not the concordant genes. Trend 11 trend encompassed 46 down-regulated genes (9 of which were discordantly expressed) active from the first day until the fifth day of RRR, when they began to return to normal levels of expression (Fig 4 and supplemented Fig 10 and Table 12).

Therefore the RRR shares with RCC two qualitative gene expression signatures: a concordant and a discordant. The genes in the two signatures are significantly subject to regulation by similar pathways as well as significantly distinct pathways ( $p < 0.05$ ). Finally, the probability of being able to observe these concordant (77% RRR/ RCC) and discordant (23% RRR/ RCC) genes merely through chance would be extremely low if RRR and RCC phenotype were unrelated ( $p$ -value  $2.2e-16$ , binomial test) (Table 4).

#### **The biological basis of concordantly and discordantly expressed genes in RRR and RCC**

In the search for the biological basis of the concordant and discordant groups, we analyzed these genes using the Gene Ontology consortium ontologies (GO), (Fisher Exact  $p < 0.05$ ), (<http://www.geneontology.org>). This method revealed that the concordant genes

were significantly involved in such molecular functions as immunoglobulin binding, ECM structural constituent conferring tensile strength activity, structural constituents of ribosomes, RNA binding, cell adhesion (mainly by RRR up-regulated genes), and selenium binding (mainly by RRR down-regulated genes). The overall concordant gene expression was up-regulated in cellular components that included the cytosolic ribosome, the proteasome core complex, collagen, the small ribosomal subunit, and the microfibril. The biological processes with an overall concordant gene up-regulated expression were DNA replication initiation, ribosome biogenesis, macromolecule biosynthesis, cytoplasm organization and biogenesis, cell death, cell adhesion, immune response, and protein metabolism. Process with mainly down-regulated concordant genes included phenylalanine metabolism and catabolism, tyrosine metabolism, and cell ion homeostasis. Other significant processes affected included regulation of translation, posttranslational membrane biomarkering, ER organization and biogenesis, and cell growth and/or maintenance (Table 5).

On the other hand, the discordant genes were significantly (Fisher Exact  $p < 0.05$ ) found in molecular functions as insulin-like growth factor binding, organic cation transporter activity, and heparin binding. The discordant genes were significant in the cellular component of extracellular space and were significantly associated with the molecular processes of one-carbon compound metabolism, angiogenesis, regulation of cell growth, actin cytoskeleton organization and biogenesis, actin filament-based processes, enzyme-linked receptor protein signaling, organelle organization and biogenesis, and organogenesis (Table 5).

Following this analysis, we then cross-compared gene ontologies (Fisher Exact  $p < 0.05$ ), among the concordant group, the discordant group, and the group continuously involved in all three patterns of RRR, which we correlated above with Sutton's four-pattern model of RRR (Sutton TA et al 2002).

During the early pattern of RRR the gene category of DNA replication initiation was significantly and distinctly present in the concordant genes and consisted of five up-regulated genes. These five genes belong to the family of minichromosome maintenance proteins (MCM) and included MCM2, MCM3, MCM4, MCM5, and MCM7. With the exception of MCM5, these genes have been reported to be up-regulated concordantly in RCC pathogenesis (Tables 6 and 9).

The discordant genes significantly shared the ontology of growth factor binding with the early pattern, and the ontology of extracellular space with the late pattern (Tables 6 and 9). During the early pattern, discordant genes in the "growth factor binding" ontology were associated with the IGF pathway. Both connective tissue growth factor (CTGF/IGFBP8) and

cysteine-rich protein 61 (CYR61) were up-regulated in RRR, while insulin-like growth factor binding proteins 1 and 3 (IGFBP1 and 3) were down-regulated in RRR. The discordant genes belonging to the late pattern ontology of extracellular space that were up-regulated in RRR and included apolipoprotein E (APOE), connective tissue growth factor (CTGF), decorin (DCN), glypican 3 (GPC3) plasminogen activator, tissue (PLAT), and thrombospondin 1 (THBS1). In contrast, growth arrest and D-damage-inducible 45 gamma (GADD45G) was down-regulated in RRR. Except for GADD45G, the genes of this group shared a pattern of expression with trends 5 and 6, which were also up-regulated in RRR at two weeks after the initial trauma (Tables 6 and 9).

Among its 46-gene complement, trend 11 contains 4 concordant ( $p > 0.05$ ) and 9 significant discordant genes ( $p < 0.0003$ ). All of these genes proved to be down-regulated in RRR and included superoxide dismutase 2 (SOD2), cytochrome c oxidase subunit VIc (COX6C), kinesin family member 21A (KIF21A), kallikrein 1 (KLK1), heat shock 105kDa/110kDa protein 1 (HSPH1), carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1), methionine adenosyltransferase II, alpha (MAT2A), PCTAIRE protein kinase 3 (PCTK3), and serine hydroxymethyltransferase 2 (SHMT2). The last four genes were also regulated by the VHL pathway (Fig4, Table 5).

We then extended the gene ontologies (Fisher Exact  $p < 0.05$ ) to a cross-comparison with the following groups: total gene-expression data, the sub-sets for early and/or late RRR, expression trends, pathways such as IGF, concordance and discordance with RCC (Figs. 6 A-C, Tables 4, 5).

The concordant genes and trend 2 (up-regulated in the early RRR and moderately down regulated at the late RRR) corresponded primarily with ontologies of ribosome and defense (Fig. 6 A-B). Possibly, a sub-set of this pattern was also involved in the Hypoxia and VHL pathways, and trend 4, which was up-regulated during early RRR, but returning to normal expression levels at two weeks of RRR (Fig. 6 A-B). P53 and NF-kB were regulating ontologies in defense/ immune responses, death process and ER genes (Fig. 6 A-B).

The ontologies involved in the IGF pathway were also present in the genes discordantly expressed between RCC and RRR. These included such processes as cell growth and angiogenesis and functions as growth factor binding, enzymatic reactions, glycosaminoglycan binding, and heparin binding. Finally, certain cellular components, including ECM, were co-represented in both the IGF pathway and the RCC discordant gene subset. Because both the IGF pathway and the discordant gene subset share genes to a significant degree, we suggest that the IGF pathway plays a functional role in RRR and RCC (Fig 6 A, C).

Even this comprehensive probabilistic analysis may fail to capture many key aspects of discordant gene function. To mitigate this possibility, we also catalogued the discordant genes on a non-probabilistic, gene-by-gene basis (Table 7). Most of the changed genes in the discordant group belong to subgroups that are important in maintaining cell structure, gene expression, ECM function, angiogenesis, DNA repair, catabolism, mitochondrial functions, motility, catalytic activity, stress signals, external signals, ubiquitination, immunity, oxidation, metastasis, migration, and adhesion. Similarly to the results of our previous analysis (Table 4), genes regulated discordantly when comparing normal RRR and RCC, proved or suggested to be regulated by the IGF, VHL-HIF, hypoxia, C-MYC, p53, or NF-kB pathways. Moreover, some of these genes are known to play roles in pathways involved in senescence, tumor suppression, or oncogenesis.

We next utilized probabilistic functional genomics to complement the comparison of the concordantly and discordantly expressed genes between RRR and RCC (the full and comprehensive probabilistic functional genomics analysis is currently under preparation for publication). Of great interest is the enrichment for the ARNT (HIF-1b) homodimer element in the promoter regions of the concordant genes (loading of -4.169418). 21 concordantly expressed genes were up-regulated and 9 genes down regulated and included continuously, early and late expressed genes (Table 8). Also, 6 discordantly expressed genes were suggested to have the ARNT homodimer element, one of which is EglN1.

We pursued a cross-comparative approach in analyzing gene expression patterns and regulatory mechanisms implicated in wound healing and/or RCC pathogenesis. We observed a high degree of concordance among the genes differentially expressed in both RRR and RCC. However, we also observed a discordant differential gene expression that differentiated the RRR and RCC and might be specific to malignant transformation. Further, we have identified gene expression programs of pathways, functions, and cellular locations that appear to play a multifaceted role in wound healing and/or carcinogenesis.

#### **Renal ischemia- reperfusion as a wound healing model**

To induce tissue regeneration in normal mouse kidney, we chose to use a unilateral renal ischemia model. The predominant consequences of renal injury in this model include proximal tubule necrosis, as well as apoptosis in a minority of the cells. The reversal of these changes coincides with the reestablishment of the normal renal epithelial barrier as new cells reline the denuded tubules (Price, P.M. et al., 2003). Wound healing is a complex, but orderly phenomenon involving a number of principle processes: induction of acute inflammatory processes by the initial injury; regeneration of parenchymal cells; migration and proliferation

of parenchymal and connective tissue cells; synthesis of ECM proteins; remodeling of connective tissue and parenchymal components; and finally, collagenization and acquisition of wound tensile strength (Cotran, R.S. et al., 1999). Regions of hypoxia are common in healing wounds, and the state of hypoxia alters the activity of selected transcription factors, including HIF-1 $\alpha$ , HIF-2 $\alpha$ , JNK, NF- $\kappa$ B, c-MYC, IGF, and p53. These transcriptional activations result in increased expression of growth factors, growth factor receptors, and angiogenic factors (Tables 2, 3, 9), (Elson D.A. et al., 2000, Maxwell PH. 2004, Schips L et al 2004, Hammerman MR 1999, Yamaguchi S et al 2003, Koshiji M et al 2004, Schmid T et al 2004, Qi H and Ohh M 2004, Cao CC et al 2004).

### Patterns of differentially expressed genes in RRR

Using global gene expression analysis, we have demonstrated that RRR characterized by three general patterns of differentially expressed genes referred to as “early,” “late,” and “continuous,” which includes early and late events (Fig 3, Table 1).

In terms of Sutton’s renal RRR model (Sutton TA et al 2002)—initiation, extension, maintenance, and repair—the “continuous” (early and late) pattern we have defined encompasses gene functions relating to all four patterns. The “early” pattern subsumes functions related to initiation, extension, and early maintenance, while our “late” pattern of RRR includes maintenance as well as recovery. Our data supports a model of ischemic RRR as a complex, but orderly continuum composed of overlapping patterns that continuously up-regulate the immune response and down-regulate oxidoreductase activity. Gene functions relating to dedifferentiation, migration, proliferation, redifferentiation, and repolarization are associated with the maintenance and repair patterns in Sutton’s model. Refining this, we have observed that during early RRR, the regulated genes are involved in cell proliferation and only during late RRR do genes implicated in redifferentiation become differentially expressed (Table 2).

### Normal RRR processes are found in RCC

Through the comparative analysis of global gene expression patterns characteristic of RRR and RCC, we have identified a total of 361 genes implicated in one or both processes, as well as global regulatory patterns that are shared concordantly (278 genes) or discordantly (83 genes) between renal wound healing (RRR) and carcinoma (RCC). The probability of observing such an ensemble of concordant and discordant genetic activity by chance would be highly unlikely if RRR and RCC phenotypes were unrelated (p-value  $2.2 \times 10^{-16}$ , binomial test) (Fig 5, Table 4).

Concordant genes comprised the majority (77%) of the 361 genes we identified; most of the genes in this group were related to processes involved in renal cell maintenance, including metabolic functioning, DNA replication, cellular defense, immune response and cell death (Table 5).

DNA replication is an essential step in both normal and transformed dividing cell. We found that four members of the highly conserved mini-chromosome maintenance (MCM2, 3, 4 and 7) protein family are concordantly up-regulated during the early pattern of RRR and in RCC ( $p < 0.05$ ). A fifth member, MCM5 is also up-regulated during the early pattern of RRR, but the expression in RCC needs to be tested. The complex formed by MCM proteins is a key component of the pre-replication complex and may be involved in the formation of replication forks and the recruitment of other DNA-replication-related proteins.

The concordantly expressed genes also include 167 genes that retained the normal renal cell program of apoptosis (Table 5) and may thus indicate that the apoptotic mechanism is partially maintained in RCC. Furthermore, we observed that the anti-apoptotic and anti-inflammatory gene heme oxygenase-1 (HO-1/ HMOX1) is up-regulated in both RRR and RCC; thus, it is possible, perhaps probable, that the up-regulated gene contributes to cytoprotection during each process (Goodman A.I. et al., 1997, Adachi S et al., 2004).

Our probabilistic functional genomics comparison of the concordantly with the discordantly expressed genes between RRR and RCC, suggests an enrichment for the binding element for the transcription factor ARNT in the promotor of the concordat genes and not the discordant genes (Table 8). ARNT functions as a potent coactivator of estrogen receptor-dependent transcription and has also been identified as the beta subunit of a heterodimeric transcription factor, HIF-1a (Brunnberg S et al 2003).

#### **Significant normal RRR pathways and processes are discordant in RCC**

The discordant genes were a distinct minority of the genes shared between RRR and RCC (23%). These include apparent pathogenesis-related genes and background noise due to the differences in organisms, tissue pathologies, methods and authors (see the on-line appendix). A GO analysis predicted that the discordant genes were to play a significant major role in insulin-like growth factor binding, heparin binding, the renal extracellular space and in organic cation transporter activity ( $p < 0.05$ ). These ontologies were distinctly different from those predicted for the concordant genes and thus we expect the concordant and discordant genes to be functionally different (Tables 5, 6, 7, Fig 6). We have also identified a set of critical discordantly expressed genes associated with pathways or functions that may be required for RCC pathogenesis. Among these pathways and functions are the IGF pathway

(observed as ontology as well), the HIF-VHL pathway, which is interconnected with the IGF pathway and processes as angiogenesis, fatty acid metabolism, glycolysis and ATP synthesis, mitochondrial, apoptosis, DNA repair and mRNA maturation. The significance of these changes is discussed below in the context of basic tumor biology.

EASE (<http://apps1.miaid.nih.gov/David/>), analysis was performed on significant genes (Hosack DA et al., 2003). EASE uses a Fisher Exact test to estimate significance for functional classes of genes in a significant subset relative to the representation on the array. Gene ontology (GO) terms for biological process, cellular component, and molecular function were used (<http://www.geneontology.org>). The ontologies were crossed compared by using a macro that we wrote in Excel and Michael Eisen Cluster program

### The IGF pathway

We discovered that the discordant genes significantly share the ontology of insulin-like growth factor 1 (IGF-1) with the early pattern of RRR (tables 5, 6). This finding, obtained through GO analysis, is strongly supported by the literature and points to a significant regulatory role for the IGF-HIF-VHL pathways (Tables 4, 7, 9, Fig 6). We found that IGFBP-1, -3 and -4 are down-regulated during the early pattern of RRR. In our study IGF-1R was not printed on the array, but in the with the literature was reported as down-regulated, unchanged and up-regulated in RRR, possibly influenced by the type and severity of the renal injury and the nutritional intake of the animal (Bohe J. et al 1998). Discordantly, in RCC the expressions of IGFBP-1, -3 and IGF-1R are up-regulated, a phenomenon that could in part, be attributed to the up-regulation of the HIF1a protein as a result of the loss of VHL (Table 9), (Schipis L et al (2004)). Another discordantly expressed IGF-1 weakly-binding-protein was CTGF (IGFBP-8), which was up-regulated during the late pattern of RRR, but down-regulated in RCC. CTGF has the capacity to bind IGF-1 via its IGF-binding domain, albeit with relatively low affinity compared with classical IGFBPs. CTGF and IGF-1 cooperate in their upregulation of collagen type I and III expression in human renal fibroblasts. The synergy between CTGF and IGF-I might be involved in glucose-induced matrix accumulation, because both factors are induced by hyperglycemia (Lam S et al 2004).

The IGF1 signaling pathway controls cellular proliferation and apoptosis, and high levels of circulating IGF-1 are associated with increased RRR and risk of several common cancers (Bohe J. et al 1998, Pollak MN et al 2004). There is a profound body of evidence to suggest that the neoplastic progression, particularly in RCC, might be associated with increased expression of IGF-1 and the receptor for IGF-1 (IGF-1R) (Parker AS et al 2003, Schipis L et al (2004)). The expression of IGF-1 together with its receptor, IGF-1R, provides

evidence for the existence of an autocrine-paracrine loop of tumor cell stimulation in RCC and makes this type of cancer a candidate for therapeutic strategies aimed to interfere with the IGF pathway (Schipis L et al (2004)). IGF-1 bioavailability is modulated by IGF binding proteins (IGFBPs) in both the circulation and the cellular microenvironment. There are opposing models regarding the regulatory role of IGFBPs in IGF-1-induced mitogenic activity. The simplest suggests that IGFBs act as competitive inhibitors which deprive receptors of their ligands (Pollak MN et al 2004). An alternative model claims that IGFBPs can enhance neoplastic behavior, while reduced IGFBPs expression can inhibit tumor growth (Pollak MN et al 2004, Renehan AG et al 2004, Dupont J et al 2003).

#### 0 The HIF-VHL pathway

The majority of kidney cancers are caused by the mutation of the von Hippel-Lindau (VHL) tumor suppressor gene. The VHL protein (pVHL) is part of an E3 ubiquitin ligase complex called VEC that is composed of elongin B, elongin C, cullin 2, NEDD8, and Rbx1. VEC biomarkers a HIF transcription factor for ubiquitin-mediated destruction by oxygen-dependent prolyl hydroxylation (PHD1, 2, 3/ EGLN 2, 1, 3). In the absence of wild-type pVHL--as occurs in both VHL patients and the majority of sporadic cases of clear cell renal cell carcinoma—HIF-responsive genes are inappropriately activated under normoxic conditions (Sufan RI et al 2004).

Following renal ischemia injury, we found 17 genes to be HIF-responsive in the processes of RRR ( $p < 0.05$ ), 7 of which proved to be discordantly expressed in RCC ( $p < 0.05$ ), (Table 4, 5). Interestingly, another discordant genes we identified are the PHD2/ EGLN1 and PHD3/ EGLN3 which are up-regulated in RCC (Jiang Y et al (2003), Boer et al (2001)), but down-regulated together with EGLN2 throughout the RRR process (Table 9, Fig 9). Based on our probabilistic promoter analysis of the differentially expressed genes associated with RRR (data not shown), we suggest that PHD2/ EGLN1 down-regulation may be attributed to thyrotrophic embryonic factor TEF/VBP, a transcription factor that regulates developmental stage-specific gene expression. TEF has been shown to be closely related to the HLF of the E2A-HLF fusion gene, formed by a (17;19)(q22;p13) translocation (Inaba T et al 1992). This fusion product binds to its DNA recognition site not only as a homodimer but also as a heterodimer with TEF (Inukai T et al 1997). Thus, TEF could possibly play oncogenic roles in both the HIF pathway and E2A-HLF activity.

Another discordantly expressed gene belonging to the HIF pathway that was identified in our study is the WD repeat and SOCS box-containing 1 (WSB1, RIKEN 2700038M07 gene pending), which is up-regulated during the late pattern of RRR, but down-regulated in RCC.



Kamura T. et al. have shown that VEC, SOCS1, and WSB1 are capable of assembling with the Cul5/Rbx1 complex. Cul5 and Cdc34 are HIF1a, E2 ubiquitin-conjugating enzymes (Kamura T et al 2001). Thus, the even though EGLN1 and 3 are up-regulated in RCC, the down-regulation of WSB1 may impair assembly with the Cul5/Rbx1 and therefore ubiquitylation by the E2 ubiquitin-conjugating enzyme Ubc5.

We also found a discordant gene, UBE2V1/CIR1, which is a variant of the ubiquitin-conjugating E2 enzyme. UBE2V1 is thought to be involved in the control of differentiation by altering cell-cycle behavior. Up-regulation of UBE2V1 expression has been found following cell immortalization in RCC and in tumor-derived human cell lines (Ma L et al 1998). We found that this enzyme is down-regulated throughout the process of RRR. Further studies are needed to explore the connection, if any, with the HIF1a, E2 ubiquitin-conjugating enzymes, Cul5 and Cdc34.

The histone deacetylase 1 (HDAC1) expression is down regulated during the late pattern of RRR and is yet to be examined in RCC. Several lines of evidence suggest that HDAC expression in up-regulated in RCC. The HIF1 complex is often over expressed in RCC because of the loss of the VHL protein and hypoxia. Under these conditions HDAC expression is expected to be up-regulated, possibly by the regulation of the HIF1 transcription complex (Kim, MS et al (2001)). Importantly, patients with renal cell carcinoma and other tumors treated with HDAC inhibitors showed some degree of clinical improvement (Sasakawa Y et al (2003), Drummond DC et al (2004)). The association of VHL protein with HDAC-1, HDAC-2, and HDAC-3 provides a molecular basis for the repression of the HIF1a transactivation domain function under nonhypoxic conditions. Interestingly, HDAC1 mRNA and protein expression are induced by hypoxia, suggesting that HDAC1 may represent a HIF-1 biomarker gene and that increased HDAC activity may contribute to the overall decreased rate of transcription in hypoxic cells (Kim MS et al. (2001), Mahon PC et al (2001)). Further, the HDAC interacts with retinoblastoma tumor-suppressor protein and this complex is a key element in the control of cell proliferation and differentiation. Together with metastasis-associated protein-2, it deacetylates p53 and modulates its effect on cell growth and apoptosis. (Luo, J et al 2000, Magnaghi-Jaulin, L et al (1998)). Interestingly, another histone deacetylase gene that we observed in our study is the Sirtuin 7 (SIRT7), which is discussed with respect to DNA repair. SIRT7 is presumably also a discordant gene and in cultured neuronal cells is reported to be up-regulated following modification of histone/protein acetylation status by several class I and II HDAC inhibitors (Kyrylenko S et al (2003)). The biological role of

HDAC1 is epigenetic and complex, but the net effect of HDAC1 over-expression is to stimulate angiogenesis and control of cell proliferation and differentiation.

A novel pathway that specifically suppresses downstream HIF-1 signaling by stress granules has recently been identified by Moeller BJ et al (2004). In these granules, the up-regulation of the key stress granule scaffolding proteins, TIA1 cytotoxic granule-associated RNA binding protein (TIA1) and TIA1 cytotoxic granule-associated RNA binding protein-like 1 (TIAL1/ TIAR), results in hypoxia-mediated translational decrease. In contrast, in the presence of free radical species (ROS) the stress granules depolymerizes, the downstream HIF-1 signaling is enhanced, leading to increased translation of HIF-1-regulated transcripts as VEGF. ROS is formed following radiation therapy, RCC pathogenesis and RRR and thus HIF translational silencing is expected to be impaired. During early RRR, TIAL1 is up-regulated and presumably involved in gene transcriptional silencing. During late RRR TIAL1 expression reverts to normal levels, thus mediating the translation of HIF-1-regulated transcripts.

We also found that the gene Nulp1 (KIAA1049), a basic helix-loop-helix protein, is discordantly expressed. Nulp1 is down-regulated during early RRR, but is up-regulated both in RCC and during early embryonic organogenesis (Table 9) (Olsson M et al 2002). Interestingly, Nulp1 and ARNT (HIF-1b) proteins can bind to and activate transcription from promoters driven by the CACGTG E-Box element. This activation is potentially repressed by the HIF regulated inhibitor of D binding 2 (ID2), which is concordantly up-regulated in RCC and at the late pattern of RRR (Table 9). (Scobey MJ 2004, Lofstedt T et al 2004).

HIF1 activates the transcription of genes that are involved in crucial aspects of cancer biology, including angiogenesis, cell survival, glucose metabolism and invasion (Semenza GL 2003). Both intratumoral hypoxia and the genetic alterations induced by the genetic discordantly expressed genes discussed above can lead to HIF1a overexpression, which has been associated with increased patient mortality in several cancer types, including RCC.

### Angiogenesis

Tumor angiogenesis differs significantly from normal angiogenic processes several important respects, including aberrant vascular structure, altered endothelial-cell-pericyte interactions, abnormal blood flow, increased permeability, and delayed maturation. The onset of angiogenesis, or the "angiogenic switch," is a discrete step that can occur at any stage of tumor progression, depending upon the tumor type and characteristics of its microenvironment (Bergers G, Benjamin LE. (2003)). In RCC, the angiogenic factor VEGFA and its receptor KDR/VEGFR2 are up-regulated, but both genes are down-regulated at the early pattern of

RRR and VEGF throughout the late pattern as well (Table 7). These findings are supported by the reports that in RRR --unlike in other organs-- VEGF is primarily up-regulated at the post-transcriptional level (Vannay A et al (2004), Kanellis J et al (2000), Lemos FB et al (2003)). On the other hand, the endothelial VEGFR2, but not VEGFR1, was reported earlier to be up-regulated in rats RRR (Kanellis J et al (2000)). Hypoxia-dependent VEGF up-regulation in carcinoma is attributed to the up-regulation in HIF1a protein consequent to the loss of VHL, and VEGF down-regulation in wound healing could result from a synergistic interaction among multiple regulatory transcription factors and/or inhibitors capable of overcoming HIF1a induction (Fig 7, Table 9). These observations indicate that the discordant expression of the pro-angiogenic genes VEGFA and KDR are very likely to play a central role as an onco- angiogenic switch during RCC pathogenesis.

#### **Fatty acid metabolism**

Fatty acid metabolism plays a major role in cancer. Our study found that two fatty acid metabolic enzymes, Acyl-Coenzyme A oxidase 1 (ACOX1/1.3.3.6) and Carnitine PalmitoylTransferase 1A (liver) (CPT1A/ 2.3.1.21) are up-regulated in RCC, but down-regulated during the late pattern or continually during RRR (respectively). The over-expression of both enzymes may increase the levels of intracellular H<sub>2</sub>O<sub>2</sub> and therefore may act analogously to other carcinogenic ROS (Okamoto M, et al 1997).

#### **Glycolysis and ATP synthesis**

Fast-growing tumors depend largely upon glycolysis for ATP generation. In hypoxic solid tumors, ATP is replenished through glucose oxidation by the anaerobic glycolytic pathway, even though this pathway is far less effective in ATP production than is aerobic glucose oxidation (Frydman, B. et al., 2004). Our comparison between RCC and RRR indicates major differences in the expression of certain glycolytic genes:

The enzymes hexokinase 1 (HK1) but down-regulated during early RRR. HK1 phosphorylate glucose produces glucose-6-phosphate, thus in RCC committing glucose to the glycolytic pathway (Tables 7, 9). Another enzyme in the glycolytic pathway, the phosphofructokinase Liver (PFKL) proved to be down-regulated in the early pattern of RRR and its expression in RCC is yet to be determined. PFK catalyzes a key step in glycolysis, namely the conversion of D-fructose 6-phosphate to D-fructose 1,6-bisphosphate. In kidney, HK1 and PFKL are expressed in the PRT and are regulated by HIF1a and possibly by p53 (Table 9). In many tumors, HK1 and PFKL are unleashed to supply the cell with ATP (Eigenbrodt, E. et al., 1992, Nakamura, K., 1988, Semenza, G.L. et al., 1994).

To stimulate continued glycolytic flux and prevent toxic effects, lactate must be eliminated from the cell. This process is mediated by the monocarboxylate transporter (MCT). In RCC, SLC16A7/MCT2 is up-regulated, while in normal RRR it is down regulated, an observation that further supports the notion that tumor cell is programmed to maintain continued glycolytic flux and prevent toxic effects (Lin, R et al 1998; Halestrap AP and Price NT 1999).

We also found three genes associated with purine metabolism are discordantly expressed in RSS and during RRR: the fragile histidine triad (FHIT), the ribonucleotide reductase M1 polypeptide (RRM1,) and ectonucleotide pyrophosphatase/ phosphodiesterase 2 (autotaxin), (ENPP2). FHIT is inactivated in many of the common human malignant diseases and it is localized close to the renal tumor suppressor gene, VHL. FHIT is either down-regulated or deleted in RCC but highly expressed in all normal epithelial tissues and is up-regulated during RRR (Tables 7, 9).

RRM1 is up-regulated in RCC in down-regulated in the early pattern of RRR (Tables 7, 9). RRM1, also, catalyzes the activity of thioredoxin (TXN), which expression is up-regulated in RRR. The literature describing the TXN expression pattern in RCC is contradictory: some reports have indicated that the gene is down-regulated, while other studies have offered evidence suggesting that it is up-regulated (Tables 7, 9). We have found that two members of the thioredoxin family possess distinctly different expression patterns during different patterns of RRR: thioredoxin-like (TXNL) is up-regulated during the early pattern of RRR, while thioredoxin 2 (TXN2) is down-regulated during the late pattern of RRR. TXN2 plays an important role in protecting mitochondria from oxidant-induced apoptosis and its down-regulation therefore serves to switch on the apoptosis process (Chen, Y. et al., 2002). Nonetheless, we have yet to clarify the role of the differential TXN expression in RCC

Ectonucleotide Pyrophosphatase/Phosphodiesterase 2 (autotaxin), (ENPP2) is down-regulated continuously throughout the process of RRR, but elevated in RCC and other tumors (Tables 7, 9). ENPP2 is an extracellular enzyme and an autocrine motility factor that stimulates pertussis-toxin-sensitive chemotaxis in human melanoma cells at picomolar to nanomolar concentrations. ENPP2 processes 5'-Nucleotide phosphodiesterase/ ATP pyrophosphatase and ATPase activities that potentially induce tumor cell motility, and enhance experimentally induced metastasis and angiogenesis (Clair, T., et al., 2003).

During early RRR, phosphofructokinase-Liver (PFKL) is down-regulated and returns to normal levels during the late pattern of RRR (Tables 7, 9). Presumably, the rate of glycolysis is normally greatly in excess (greater than 400-fold) of that required for

biosynthetic processes. Therefore, PFKL is first down-regulated, and then restored back to the normal level or to the level that is needed to meet any new ATP demand (Newsholme EA and Board M 1991). Further studies are needed to evaluate the PFKL expression in RCC.

A localized increase in ADP, which stimulates glycolysis and ATP production is generated by the SLC1A1/ EAAC1 turnover (Welbourne and Matthews 1999). During the late pattern of RRR SLC1A1 expression is up-regulated, but in RCC, it is down-regulated. A decrease in the expression of SLC1A1 may slow the glycolysis and presumably results in further ATP deficit.

When O<sub>2</sub> is limiting, cells switch from oxidative phosphorylation to glycolysis as the primary generator of ATP (Pasteur effect). In hypoxic tumors as RCC, the constitutive stabilization of HIF in Vhl-/- cells together with the discordant expression of genes in the HIF-IGF pathway, further increases the hypoxic response of these cells. Therefore, in RCC the expression of key glycolytic genes is altered to meet the cell ATP needs. The discordant expression of these genes in RCC Vs. RRR may represent a normal glycolysis that gone awry.

## **The mitochondria**

Mitochondrial defects have been associated with neurological disorders, as well as cancers. Two ubiquitously expressed mitochondrial enzymes succinate dehydrogenase (SDH) and fumarate hydratase (FH, fumarase) catalyze sequential steps in the TCA cycle. SDH is a component of complex II of the respiratory electron-transport chain. Germline heterozygous mutations in the autosomally encoded mitochondrial enzyme subunits SDHD, SDHC and SDHB cause the inherited syndromes pheochromocytoma and paraganglioma. In RCC the expression of the SDHB gene is down regulated, which is in concordance with the data we have derived from our RRR set indicating that SDHA and SDHB are down-regulated during the early pattern of RRR (Table 9). Partial or complete loss of SDH or FH activity leads to energy depletion, free-radical formation and is sensed by the mitochondria as hypoxia. This leads to stabilization of HIF-1, its translocation to the nucleus and activation of its biomarker genes and possibly loss of mitochondrial-mediated energy-dependent apoptosis (Eng C, et al., 2003). Once the mitochondrial outer membrane is breached or undergoes a change in composition because of the ROS, an energy-independent apoptotic cascade occurs that involves release of cytochrome c and procaspases (Eng C, et al., 2003). The gene encoding to the cytochrome c oxidase subunit VIc (COX6C), is also differentially expressed during the early pattern of RRR, where it is down-regulated, as apposed to RCC, where it is up-regulated. COX6C is a subunit of the cytochrome c oxidase (COX), the terminal enzyme of the

mitochondrial respiratory chain that catalyzes the electron transfer from reduced cytochrome c to oxygen. Thus a discordant over-expression in RCC may impact this catalysis.

These discordant genes collectively constitute the first detailed global molecular comparison of the pathways and cellular process generating the energy balance during RRR and RCC. These findings support the Warburg hypothesis suggesting that the cause of cancer is primarily a defect in energy metabolism (Warburg, O 1956). Through numerous studies it has become apparent that tumor cells rely to a greater extent on glycolytic pathways than do normal cells even in the presence of abundant oxygen. While it is clear that the metabolism of cancer cells is different from that of normal cells, our work identified the candidate genes distinguishing the metabolism of RRR from RCC.

It is conceivable that partial decreases or chronic, low-level reductions in energy production, which are insufficient to cause overt symptoms but could contribute to inefficient energy-dependent apoptosis (van Loo, G. et al 2002; Ravagnan, L. et al 2002, Eng C, et al., 2003). Thus the subsequent impact of a discordant gene in the energy balance could lead to complete loss of energy-dependent apoptosis and therefore to cancer promotion

## DNA repair

DNA repair mechanisms can be induced under a variety of physiological and pathological conditions. We identified a number of discordantly expressed genes—prominent among which are SMC1L1, TOP3B, and SIRT7—suggesting that certain alterations in DNA repair mechanisms play an important role in RCC pathogenesis discordant genes also exemplified possible alterations in the DNA repair:

The structural maintenance of chromosomes 1-like 1 (yeast) (SMC1L1), is up-regulated during the early pattern of RRR, but down-regulated in RCC (Tables 7, 9). As part of the cohesin complex, the protein encoded by SMC1L1 is essential for sister chromatid cohesion in yeast cells undergoing mitosis. In addition, the protein has a potential role in DNA repair (Sumara, I. et al 2000).

Another discordantly expressed gene involved in DNA repair was the topoisomerase (DNA) III beta (TOP3B), that is down-regulated during the early pattern of RRR, but up-regulated in RCC (Tables 7, 9). This gene encodes a DNA topoisomerase, an enzyme that controls and alters the topologic state of DNA during transcription. The TOP3B enzyme catalyzes the transient breaking and rejoining of a single strand of DNA, allowing the strands

to pass through one another, by relaxing the supercoils and altering the topology of DNA. The enzyme interacts with DNA helicase SGS1 and plays a role in DNA recombination, cellular aging, and the maintenance of genome stability (Li W and Wang JC 1998).

Sirtuin 7 (SIRT7) may represent another discordantly expressed DNA repair gene involved in RCC pathogenesis, but it needs to be studied further before such a role can be confirmed. We observed that SIRT7 is down-regulated at the early pattern of RRR (Table 9). We have gathered evidence that the gene is up-regulated in carcinoma of the thyroid but have yet to acquire data confirming that it is similarly up-regulated in RCC. Sirt7 is a member of the sirtuin family of proteins, which are homologs of the yeast Sir2 proteins (Sir1-7). The functions of human sirtuins have not yet been determined; however, yeast sirtuin proteins are associated with calorie intake, regulation of metabolic rates, chromatin regulation, and DNA recombination. It has been suggested that SIRT 1 promotes the long-term survival of irreplaceable cells (North BJ et al 2004, North BJ et al 2004, Cohen HY et al 2004). Thus discordant expression of genes involved in DNA repair could result in accumulation of mutations and genome instability.

#### **mRNA maturation**

One of the key events that takes place in the nucleus during mRNA maturation is the polyadenylation of the 3-prime end of eukaryotic mRNA. We observed that the poly(A) polymerase (PAPOLA/PAP) is continuously down-regulated throughout the process of RRR, but up-regulated in RCC (Table 9). This discordant gene is of particular interest as high levels of PAPOLA activity are associated with rapidly proliferating cells, the enzyme exerts anti-apoptotic effects and it has been identified as an unfavorable prognostic indicator in leukemia and renal cancer (Stetler DA et al 1981, Balatsos NA et al 2000). Thus, we suggest that the discordant genes are also involved in the deregulation of mRNA in the tumor cells.

#### **The extracellular space**

Our set of discordant genes also significantly shared the ontology of the ECM. We found five of the six genes in this ontology to be up-regulated, with a pattern of expression similar/identical to that of trends 5 and 6, both of which are up-regulated at two weeks (Tables 5, 6, 7, 9, Fig 6). Normal cells remain confined to their home territory because they are held in check through an interchange of signals with neighboring cells and the surrounding ECM. In contrast, successful malignant tumor cells have been hypothesized as being resistant to such regulatory signals as a result of appropriating, misinterpreting, or disregarding the signals during the invasion of local host-cell populations (Liotta LA and Kohn EC. (2001)).

The ECM genes we found to be up-regulated during the late pattern of RRR, but down-regulated in RCC--APOE, CTGF/IGFBP8, DCN, GPC3, PLAT, and THBS1—all appear to be play distinct roles in the malignant cell's complex process of becoming resistant to regulatory signals originating from surrounding cells and/or the ECM.

Down-regulation of APOE appears to slow microtubule polymerization *in vitro* (Scott BL et al 1998), and thus may affect the growth and behavior of malignant cells as in RCC tumor (Lenburg ME et al (2003), Boer JM et al (2001), Galban S et al (2003), Vogel T et al 1994, Ishigami M et al 1998). Down-regulation of CTGF may inhibit CTGF induced mesangial cell migration in RCC (Crean JK et al 2004).

DCN, the third discordant ECM gene, encodes the pericellular matrix proteoglycan, decorin, a protein component of connective tissue that binds to type I collagen fibrils. It plays a role in matrix assembly and is capable of suppressing the growth of various tumor cell lines (Moscatello, DK et al 1998).

Mutations in the fourth discordantly down-regulated gene, GPC3, may have a possible role of in Wilms tumor development and in an overgrowth disorder, Simpson-Golabi-Behmel syndrome, that may be independent of IGF signaling (White GR et al 2002; Lindsay S et al 1997, Chiao E et al 2002).

The fifth gene, PLAT, is a serine protease that activates the proenzyme plasminogen to yield plasmin, which has fibrinolytic activity. Increased plasmin activity causes hyperfibrinolysis, which manifests as excessive bleeding; decreased activity leads to hypofibrinolysis, which can result in thrombosis or embolism (Jorgensen et al. (1982)).

The final gene of this group, THBS1, encodes an adhesive glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. The protein has been shown to play roles in platelet aggregation, angiogenesis, and tumorigenesis. Moreover, IGF2 over-expression a common genetic alteration of adrenocortical carcinomas, has been significantly correlated with both higher VEGFA and lower THBS1 concentrations (De Fraipont et al. (2000)).

#### **The organic cation transporter**

The organic cation transporter, solute carrier family 22 (SLC22A1), is critical for the elimination of many endogenous small organic cations, as well as a wide range of drugs and environmental toxins, in kidney and other tissues. SLC22A1 is up-regulated in RCC, but down-regulated in RRR (Fig 9). It may play a role in eliminating toxins— and possibly anticancer—drugs from carcinoma cells but lack an analogous function in normally regenerating kidney cells (Shu et al. (2003)).



### Specific pathways are activated during RRR and in RCC

In both RCC and healing wounds, hypoxia alters overall cellular behavior as a consequence of, or in addition to, activating specific genetic pathways, such as HIF-VHL, MYC, p53, IGF and NF-kB (Elson D.A. et al., 2000, Maxwell PH. 2004, Schips L et al 2004, Hammerman MR 1999, Yamaguchi S et al 2003, Koshiji M et al 2004, Schmid T et al 2004, Qi H and Ohh M 2004, Cao CC et al 2004) (Table 4, Figs 5,6). Our observations have shown that several concordantly expressed genes are significantly regulated by hypoxia and the pathways of VHL Myc, p53 and NF-kB, but not by the interconnected pathways of IGF and HIF ( $P < 0.05$ ). These findings indicate that the VHL gene plays a significant role not only in HIF-dependent pathways, but also in some pathways independent of HIF (Wykoff CC et al 2004). Added to this observations, our probabilistic functional genomics comparison of the concordantly and discordantly expressed genes between RRR and RCC (Table 8) suggests a distinct enrichment (loading of -4.169418) of ARNT homodimer element (5'-CACGTG-3') in the predicted promotor region regulating the expression of the concordant genes (30 genes) and less in the discordant genes (6 genes). 7 genes, 6 of them concordantly expressed were reported in the literature to be regulated by Myc (Table 8). The c-Myc/Max heterocomplex and the ARNT/ARNT heterocomplex interact to the same DNA recognition but with different affinity (Swanson HI and Yang JH 1999). ARNT proved to be capable of homodimerizing as well participating in multiple partnerships resulting in a diversity of DNA recognition sites. Partners of ARNT include AHR, SIM1, SIM2, HIF-1a, HIF-2a and CHFI, regulators of xenobiotic-metabolizing enzymes (as cytochrome P450), neurogenesis, the cellular response to hypoxia and cardiovascular angiogenesis, respectively. In this manner, ARNT serves as a central player in regulating these divergent signaling pathways (Swanson HI (2002)).

In comparison to the concordantly expressed genes, the discordantly expressed genes are also significantly regulated by hypoxia and the pathways of Myc and p53, but not by the NF-kB. Moreover, while ARNT homodimer is distinctly enriched to be a regulator of the concordantly expressed genes, the discordantly expressed genes are distinctly regulated by the ARNT heterodimer with HIF-1a pathway regulated by IGF and VHL pathways (Tables 4, 7 and 8). Further, it is implied from our promotor analysis that EGLN1, which is involved in HIF-1a and HIF-2b ubiquitination, is subject to regulation by the ARNT homodimer.

To better comprehend the complexity of the intricate bioregulatory network we have been studying, we have formulated a Molecular Interaction Map that integrates the pathways we have extrapolated from ontology studies, probabilistic functional genomics analysis, and our survey of the literature (Fig 7). This core map (Riss, J., Kohn, K.W., et al., 2004- review

in preparation) demonstrates that normal and oncogenic regeneration are regulated by the same pathways and that the failure of a critical angiogenic master switch can provide the transformed cell with a selective growth advantage. Among these pathways are the VHL-HIF1a, IGF, Myc, P53, NF-kB and others that provide the biosystem with functional redundancy, which is enabled by cellular heterogeneity, and feedback-control systems that are used to facilitate survival in hazardous environments, such as those resulting from some anticancer drugs or hypoxia) (Kitano, H., 2004).

#### Perspective and Future Work

To our knowledge, we have described for the first time, a coherent set of molecular similarities and differences between normal RRR and RCC that, taken together, suggest the existence of a novel molecular mechanism as the aberration of a normal phenotype rather than as a lapse into chaos. The molecular aberration is in gene mutations (i.e. VHL), transcription control (i.e. the discordantly expressed PHDs genes in the VHL-HIF-1a-ARNT pathway), in the autocrine-paracrine loop regulation of tumor cell stimulation (i.e. the discordantly expressed IGFBP-1, -3, genes) and epigenetically (possibly discordant expression of the Sirt-7 and HDAC genes). The molecular aberrations lead to phenotypic aberrations in vital denominators of RRR and RCC, as in DNA repair, mRNA maturation, glycolysis and ATP synthesis, fatty acid metabolism, mitochondria, extracellular space and organic cation transporter. Collectively the phenotypic aberrations offer growth advantage needed for the RCC.

Such an insight proves of great utility in the development of therapeutic strategies to treat cancer. For example, it is possible that genes expressed concordantly in RRR and RCC may permit the tumor to respond to certain physiological signals that are known inhibit tissue regeneration. Therapeutic agents similar to such signaling molecules (i.e., initiation of DNA replication) could be developed and would perhaps have effects that would be more predictable and consistent than those of conventional agents. A few such agents are now under investigation (Riss J et al 2005, manuscript in preparation).

Another highly tempting biomarkers for intervention include the discordantly expressed genes that distinguish RRR from RCC. These genes could become the basis for biomarkering the drugs to the tumor cells, but not the normal regenerating cells (Riss J et al 2005, manuscript in preparation). Another highly tempting biomarkers for intervention include the discordant bioenergetic balance in the tumor cell (Kribben A et al 2003; Agteresch HJ et al 1999). Further, the discordantly expressed genes could also become the basis for the development of

improved RCC biomarkers for early detection and diagnosis (Riss J et al 2005, manuscript in preparation).

Finally, the findings presented here may have implications for the improved treatment of other diseases or disorders as ARF, kidney transplantation and possibly other types of malignant neoplasms that have been described in the literature as associated with trauma, chronic wounding, and inflammation.

### **Implementation of comparative biology in the current study**

#### **RRR vs. RCC**

RRR though common in human (i.e. kidney transplantation) is extremely difficult for obtaining time course viable samples. Therefore, the changes in RRR gene expression are evident from rodent models and have been less systematically studied in human. Alternatively, to the best of our knowledge no mouse model is available for sporadic RCC (). This hurdle can be overcome by a careful comparative biology analysis of the uniformity and diversity in the gene expression of RRR and RCC of mouse and human (respectively).

In the current study we integrated data from different organisms, tissue pathologies, methods and authors. The interspecies comparison of gene expression of mouse RRR with human RCC was feasible by using the normal tissue in each original publication as a reference point. The significance of the differentially expressed genes was as offered by the authors.

The feasibility of the comparison was supported by the findings that both the RCC and the RRR process are predominantly found in the proximal tubules (Fig 2), (Price, P.M. et al., 2003 Add ref for RCC). Therefore, and based on the literature, many genes in the current data set were also cataloged for their tissue topological expression (Table 9). In terms of cell replication, both tumors and regenerating tissue contain four populations of cells: (1) cycling cells, (2) cells that can be recruited into cycling, (3) cells unable to divide because they are partially differentiated and (4) dying or apoptotic cells (Stell, 1967, 1977).

#### **Noise reduction**

To reduce the noise in the results of the interspecies extrapolation, the differential expression was catalogued and compared only qualitatively (not quantitatively), as expressed up or down from normal tissue (Fig 9). Therefore the interspecies extrapolation of differentially expressed genes in mouse RRR and human RCC identified a core signature, which collectively (concordant and discordant genes) is conserved through both evolution and renal pathologies.

The concordance and discordance qualitative expression is a result of the inherent similarities and differences between mouse, human, RRR and RCC. The concordance between mouse RRR and human RCC at 77% supports comparability of data across species and pathologies, while the discordance at 23% indicate the difference between mouse RRR and human RCC. Both groups of genes clustered into distinct ontologies pathways and were mostly in agreement with the literature ( $p < 0.05$ ). The significance for concordant and discordant genes is high (p-value  $2.2e-16$ , binomial test).

Finally, we validated our RRR data set by comparing it with the literature, QPCR and immunohistochemistry (Table 9, Figs 2, 9). The comparison with the literature clearly demonstrated the power of using the normal tissue as a reference point. A comparison of the RRR literature with the current RRR dataset identified 91 genes that appeared on both lists. 89% of these genes were in full agreement with the literature, despite the difference in organisms (human, rat, mouse) and methods (Table 9).

Therefore, qualitative data integration is plausible if the normal tissue is used as a reference point and is subject to filtering for qualitative gene expression that is conserved in evolution and further widely correlated with the literature and or experiments.

#### Comparison of literature knowledge and our experimental data

To incorporate into our analysis the literature knowledge on RRR and RCC, we catalogued and referred these data. First we gathered the known genes to participate in pathways of the genes: von Hippel-Lindau (VHL), HIF, insulin-like growth factor (IGF), tumor protein p53 (TP53), nuclear factor of kappa light polypeptide gene enhancer in B-cells (NF- $\kappa$ B), the v-myc myelocytomatosis viral oncogene homolog (MYC) and the genes in the purine metabolism pathway. Then, we catalogued the genes that were reported to be differentially expressed in hypoxia versus normoxia, as well as the genes presumably involved in cell senescence. These are two of the major physiologic conditions in cancer and tissue regeneration and are of much interest for further studies. Next, we cataloged the known genes to be differentially expressed in pathologies as RCC, RRR, and metastasis and those suggested to be involved in pathways on oncogenes and/or tumor suppressors. Last, we referenced the literature knowledge on genes expression and renal histology. These databases were compared with the current RRR dataset and a comprehensive cross-comparison is presented in table 9.

#### Validation of the microarray dataset

A global knowledge step toward constructing a RRR systems biology network model is to build a comprehensive RRR expression database. Therefore we reviewed the evidence reported in the literature on differentially expressed genes in RRR and the relevant pathways

and cross-compared them with the current study (table 9). Of the 1325 RRR differentially expressed genes in the current study, the expression of 91 genes was previously compared with normal kidney. The qualitative expression of 89% of the 91 genes was in full agreement and only 11% was in qualitative conflict that included the genes: NID, NRP1, ZFP36L1, TNC, MAPK1, HSPD1, HK1, NEDD4, CASP1 and UK114. These results were despite the difference in organisms (human, rat, mouse) and methods (Table 9). We further validated the data by RT-QPCR of PHD2 (EGLN1) that was at least 5-fold down-regulated in early and late regenerating kidney in comparison to resting/normal kidney. Similar expression patterns were repeated with two other related prolyl hydroxylases, PHD1 and PHD3 that were at least two-fold down-regulated (Fig 9).

Lastly, The MiB-1 high expression at 2 days was in full agreement with the array results (Table 9).

**Table 1: The RRR gene expression distribution: 14% of the genes were differentially expressed**

The GEM2 mouse cDNA array was printed with 9646 spots genes. 1350 spots, corresponding to 1325 genes differentially expressed between normal-ischemic kidneys, and regenerating kidneys. The differential gene expression is presented here as up or down in regenerating Vs normal-ischemic kidney.

	Total	% of genes (9646)	Up	Down
GEM2: printed spots	9646	100%	N.A.	N.A.
Uniquely changed	1325	14%	802	523
Early (A)	629	7%	336	293
Late (B)	373	4%	227	96
Early & late (*)	323	3%	189	134

**Table 2: An ontology analysis in timely dependent fashion: distinct and common ontologies**

The differentially expressed genes were clustered according to their pattern of expression as early, late or continually RRR. Functional ontology was analysis performed (Fisher Exact  $p < 0.05$ ). The average expression of each ontology is presented in a green to red scale; green down-regulated, red up-regulated. See the supplemented table 10 for a further detailed table

**Table 3: Association of differentially expressed genes during RRR and with known pathways of RRR**

Based on the literature, the genes in known pathways of RRR were catalogued into datasets (category). The genes in each dataset that were printed on the GEM2 array are given in column A and the differentially expressed genes are given in column B. Also given for each category the relative part from the whole differently expressed gene (1325) and from the genes belonging to that category and are printed on the array. The p value is  $p < 0.05$ .

No.	Category	Category size (No. of genes) [A]	No. of genes that are changed in renal regeneration [B]	% of all changed genes (1325 genes)	% of genes in the category [B/A]	p value
1	Total No. of genes	5796	1325	100	23	N.A.
2	VHL pathway	282	104	8	37	<0.0001
3	Hypoxia pathway	251	95	7	38	<0.0001
4	HRE target (HIF)	39	17	1	44	0.0037
5	IGF pathway	139	37	3	27	0.3341
6	Myc pathway	368	136	10	37	<0.0001
7	p53 pathway	1259	262	20	21	0.0548
8	NF- $\kappa$ B pathway	200	52	4	26	0.322

**Table 4: The differentially expressed genes in RRR and RCC are regulated similarly**

984 genes, printed on the array, were previously described to be differentially expressed in RCC from normal kidney. These genes were qualitatively crossed compared with the current microarray study identifying 1325 RRR differentially expressed genes from normal kidney. 361 genes are expressed in both RRR and RCC (A), 278 concordantly expressed genes (B), and 83 discordantly expressed genes (C).

Based on the literature, the genes in known pathways of RRR and RCC were catalogued into datasets (category). The number of genes in each dataset that were printed on the GEM2 array are given in column A; the number of differentially expressed genes are given in column B and in column C are given the number of the genes changed in both RRR and RCC. Also given for each category the relative part from the whole differently expressed gene in both RRR and RCC (361 genes), RRR (1325 genes) and from the genes belonging to that category and are printed on the array. The p-value for observing the concordance (77% reg/RCC) and the discordance (23% reg/rcc) is p-value  $< 2.2e-16$ . (see also Fig 5).

Table 4

A. A. Genes changed in both renal regeneration and RCC:								
No.	Category name	Category size (No. of genes)	No. of genes that are changed in renal regeneration (B)	No. of genes that are changed on both renal regeneration and RCC (C)	% of all the 361 genes changed on both renal regeneration and RCC	In a category: the % of renal regeneration genes that are changed on both renal regeneration and RCC (C/B)	% of all the category that is changed on both renal regeneration and RCC (C/A)	p value
1	RCC	984	161	161	100	100	57	<0.00001
2	VHL pathway	282	104	75	21	12	20	<0.00001
3	Hypoxia pathway	251	95	51	14	65	28	<0.00001
4	HIF target (HIF)	139	37	11	5	46	14	0.0351
5	IGF pathway	348	136	65	18	48	18	<0.00001
6	MyC pathway	1259	262	112	31	43	9	<0.0001
7	NF-κB pathway	200	52	24	7	46	12	0.001
B. Genes changed coordinately between renal regeneration and RCC:								
No.	Category name	Category size (No. of genes)	No. of genes that are changed in renal regeneration (B)	No. of genes that are changed on both renal regeneration and RCC (C)	% of all the 361 genes changed on both renal regeneration and RCC	In a category: the % of renal regeneration genes that are changed on both renal regeneration and RCC (C/B)	% of all the category that is changed on both renal regeneration and RCC (C/A)	p value
1	RCC	984	161	278	77	77	28	<0.00001
2	VHL pathway	282	104	59	16	57	21	<0.00001
3	Hypoxia pathway	251	95	35	10	37	14	0.2305
4	HIF target (HIF)	139	37	4	3	24	10	0.4614
5	IGF pathway	348	136	55	15	40	15	<0.00001
6	MyC pathway	1259	262	80	23	31	6	0.0043
7	NF-κB pathway	200	52	19	5	37	10	0.0017
8	NF-κB pathway	200	52					
C. Genes changed coordinately between renal regeneration and RCC:								
No.	Category name	Category size (No. of genes)	No. of genes that are changed in renal regeneration (B)	No. of genes that are changed on both renal regeneration and RCC (C)	% of all the 361 genes changed on both renal regeneration and RCC	In a category: the % of renal regeneration genes that are changed on both renal regeneration and RCC (C/B)	% of all the category that is changed on both renal regeneration and RCC (C/A)	p value
1	RCC	984	161	283	78	78	8	<0.00001
2	VHL pathway	282	104	16	5	15	6	<0.00001
3	Hypoxia pathway	251	95	16	4	17	6	<0.00001
4	HIF target (HIF)	139	37	7	2	31	6	<0.00001
5	IGF pathway	348	139	10	3	27	3	0.0551
6	MyC pathway	1259	262	32	9	12	3	0.0003
7	NF-κB pathway	200	52	5	2	10	3	0.3217

**Table 5: The differently expressed genes in both RRR and RCC exhibited distinct ontologies for the concordance Vs discordance genes**

The differentially expressed genes in both RRR and RCC were clustered according to their concordance Vs discordant change. Functional ontology was analysis performed (Fisher Exact  $p < 0.05$ ). The average expression of each ontology is presented in a green to red scale; green down-regulated, red up-regulated. The number of genes up- / down- regulated in both RRR and RCC is also given and the direction is as in RRR relative to the normal kidney. In terms of Sutton's renal RRR model (Sutton TA et al 2002-Fig 1) the ontologies are related as extension (E), maintenance (M) and repair (R). See the Table 11 for detailed information.

**Table 5**

Concordance:				
Go System	Category	No of Genes UP / DOWN	Category Average Expression	Genes Expressed in RRR Phases
Molecular Function	immunoglobulin binding	3; 0	1.103	E, M, R
	selenium binding	1; 3	-0.388	E, M, R
	extracellular matrix structural constituent conferring tensile strength activity	5; 0	0.885	E, M, R
	structural constituent of ribosome	23; 0	0.737	E, M, R
	RNA binding	27; 1	0.563	E, M, R
	cell adhesion molecule activity	11; 2	0.458	E, M, R
Cellular Component	cytosolic ribosome (sensu Eukarya)	11; 0	0.730	E, M, R
	proteasome core complex (sensu Eukarya)	4; 0	0.563	E, M, R
	collagen	5; 0	0.886	E, M, R
	small ribosomal subunit	5; 0	0.698	E, M, R
	microfibril	7; 0	1.029	E, M, R
	phenylalanine metabolism	0; 3	-1.203	E, M, R
Biological Process	phenylalanine catabolism	0; 3	-1.203	E, M, R
	tyrosine metabolism	0; 3	-1.033	E, M, R
	DNA replication initiation	4; 0	0.688	E, early M
	regulation of translation	4; 2	0.135	E, M, R
	ribosome biogenesis	10; 0	0.750	E, M, R
	posttranslational membrane targeting	5; 2	0.451	E, M, R
	cell ion homeostasis	1; 4	-0.506	E, M, R
	ER organization and biogenesis	6; 2	0.483	E, M, R
	macromolecule biosynthesis	26; 2	0.608	E, M, R
	cytoplasm organization and biogenesis	25; 4	0.656	E, M, R
	death	13; 2	0.523	E, M, R
	cell adhesion	18; 2	0.609	E, M, R
	immune response	18; 0	0.554	E, M, R
	cell growth and/or maintenance	74; 25	0.309	E, M, R
	protein metabolism	57; 8	0.542	E, M, R
Discordance:				
Go System	Category	No of Genes UP / DOWN	Category Average Expression	Genes Expressed in RRR Phases
Molecular Function	insulin-like growth factor binding	2; 2	0.088	E, M, R
	organic cation transporter activity	1; 2	-0.267	E, M, R
	heparin binding	3; 2	0.102	E, M, R
Cellular Component	extracellular space	12; 12	0.084	E, M, R
Biological Process	one-carbon compound metabolism	0; 3	-0.517	E, M, R
	angiogenesis	3; 2	0.390	E, M, R
	regulation of cell growth	2; 2	0.088	E, M, R
	actin cytoskeleton organization and biogenesis	2; 1	0.177	E, M, R
	actin filament-based process	2; 1	0.177	E, M, R
	enzyme linked receptor protein signalling pathway	3; 2	0.226	E, M, R
	organelle organization and biogenesis	3; 6	-0.216	E, M, R
	organogenesis	7; 6	0.248	E, M, R



**Table 6: The differently expressed genes in both RRR and RCC exhibited distinct ontologies that are correlated to RRR expression patterns**

The functional ontology (Fisher Exact  $p < 0.05$ ) of the differentially expressed genes in both RRR and RCC were crossed compared relative to their expression: concordantly, discordantly, patterns of expression in the current microarray dataset and in terms of Sutton's renal RRR model (Sutton TA et al 2002-Fig1), as Initiation (I), extension (E), maintenance (M) and repair (R).

**Table 7: The RRR genes in non-probabilistic in-house ontologies**

The comprehensive probabilistic analysis may fail to capture many key aspects of the discordant gene functions. Therefore, we also categorized the genes into gene-by-gene, non-probabilistic in-house ontologies.

**Table 8: Probabilistic functional genomics: ARNT regulated genes are enriched for the concordant genes and not the discordant genes**

The two group of genes, the concordantly and discordantly expressed between RRR and RRR, were analyzed for the enrichment in DNA binding elements (based on the Transfac database). One of the elements that was enriched concordant genes and not for the discordant genes is the binding site for the ARNT (HIF-1b dimmer). The up and down denote the genes that were up or down-regulated from normal kidney during RRR or in RCC. The RRR expression (Fig 3) is indicated as continues, early and late; and the RRR gene expression trend (Figs 4, 10). Also indicated if the gene was reported to be regulated by the heterodimer HIF-1 $\alpha$ /ARNT (HRE), hypoxia (H) and Myc pathway (M) (Table 9).

Table 8

Symbol	RRR expression pattern	RRR expression/ normal	RCC expression/ normal	Expression RRR/RCC	Trend	Notes
EMP3	continues	up	up	concord	14	
C1QA	continues	up	up	concord	5	
YWHAH	continues	up	up	concord	2	
ICAM1	continues	up	up	concord	2	H
COPEB	continues	up	up	concord	2	
PTMA	continues	up	up	concord	2	M
SSR4	continues	up	up	concord	6	
TCN2	continues	down	down	concord	1	
USP2	continues	down	down	concord	1	
CALB1	continues	down	down	concord	1	
RPL13A	early	up	up	concord		
MCM7	early	up	up	concord	12	
RPS19	early	up	up	concord		
MCM4	early	up	up	concord	2	H, M
CKS2	early	up	up	concord	14	M
KLF5	early	up	up	concord	8	
PSMA6	early	up	up	concord	2	M
PCBP1	early	up	up	concord	8	
FES	early	up	up	concord	12	
EIF4G2	early	up	up	concord	2	
PEC1	early	down	down	concord	3	
DDT	early	down	down	concord	1	
PIPOX	early	down	down	concord	3	
GSTT2	early	down	down	concord	3	
SELENBP1	late	down	down	concord		H
PSMB10	late	up	up	concord		
ITGA6	late	up	up	concord	12	
LAPTM5	late	up	up	concord	5	
PDGFB	late	up	up	concord	5	M
PROC	early	down	down	concord	1	
CORO1B	continues	up	down	discord	6	
APOE	late	up	down	discord	5	
KDR	early	down	up	discord	1	
SCP2	continues	down	up	discord	1	
PGK1	early	down	up	discord	1	HRE, H; m
EGLN1	early	down	up	discord	16	HRE, H

**Table 9: The RRR 1325 genes expression data and specific functional gene-clusters**

- 5      1325 unique genes were identified in the current microarray dataset. The gene expression is presented as up or down from normal-ischemic kidneys. The genes were further clustered according to RCC vs. normal kidney; renal cell culture hypoxia responsive genes vs. normoxia; HIF regulated genes; VHL, IGF, MYC, NF- $\kappa$ B pathway genes; purine pathway genes; gene expression following renal ischemia reperfusion and/or acute renal failure (ARF)
- 10    vs. normal tissue; and tissue expression pattern of renal genes (e-renal histology).

**Table 10: An ontology analysis in timely dependent fashion: distinct and common ontologies**

The differentially expressed genes were clustered according to their pattern of expression as early, late or continually RRR. Functional ontology was analysis performed

(Fisher Exact  $p < 0.05$ ). The presented ontologies are the ontology core and are hyperlinked to EMBL-EBI. The average expression of each ontology is presented in a green to red scale; green down-regulated, red up-regulated. See the supplemented Table 10 for a further detailed table

**Table 11: The differently expressed genes in both RRR and RCC exhibited distinct ontologies for the concordance Vs discordance genes**

The differentially expressed genes in both RRR and RCC were clustered according to their concordance Vs discordant change. Functional ontology was analysis performed (Fisher Exact  $p < 0.05$ ). The presented ontologies are the ontology core and are hyperlinked to EMBL-EBI. The average expression of each ontology is presented in a green to red scale; green down-regulated, red up-regulated. The number of genes up- / down- regulated in both RRR and RCC is also given and the direction is as in RRR relative to the normal kidney. In terms of Sutton's renal RRR model (Sutton TA et al 2002-Fig 1) the ontologies are related as extension (E), maintenance (M) and repair (R).

**Table 12: The significance of gene in the various expression groups: patterns, trends and pathways**

The significance of gene in the various expression patterns of early, late, continues, the 27 sub- expression trends, pathways and the concordant or discordant groups was analyzed by using the chi square test (tables 3 and 4). See methods for further explanation.

**Table 13: An ontology analysis in timely dependent fashion: distinct and common ontologies.** The differentially expressed genes were clustered according to their pattern of expression as early, late or continually RRR. Functional ontology was analysis performed ( $p < 0.05$ ). The presented ontologies are the ontology core and are hyperlinked to EMBL-EBI. The average RRR expression ( $\log_2$ ) of each ontology is presented in a green to red scale; green down-regulated, red up-regulated. The numbers and average RRR expression of up- and down- regulated genes, the category p-value and enrichment are shown as well.

	Ontology Category	Early (A)					p<0.05
		Average Expression	Total Expression UP	No Genes UP	Total Expression DOWN	No Genes DOWN	
Early(A)/ Late(B)/ Continuous (*)							
Early (A)	ATP-binding and phosphorylation- dependent chloride channel activity	-0.477	0	0	-1.4296857	3	0.021897

intramolecular isomerase activity\transposing C-C bonds	-0.723	0	0	-3.6167037	5	0.003126
cis-trans isomerase activity	0.169	1.8976128	4	-0.8812236	2	0.01318
growth factor binding	-0.452	0.383383	1	-3.0957649	5	0.021394
peptidyl-prolyl cis-trans isomerase activity	0.335	1.8976128	4	-0.2247992	1	0.046163
intramolecular isomerase activity	-0.533	0.4166733	1	-3.6167037	5	0.032366
transferase activity\transferring alkyl or aryl (other than methyl) groups	0.032	2.0043726	4	-1.7833621	3	0.022759
heat shock protein activity	0.345	2.5901036	5	-0.5213829	1	0.046307
isomerase activity	-0.181	2.6834421	6	-5.5739205	10	0.000394
lyase activity	-0.218	2.4797409	5	-5.7457532	10	0.000916
hydrogen ion transporter activity	-0.441	0	0	-4.408021	10	0.032021
magnesium ion binding	-0.144	1.4708483	3	-3.0511803	8	0.028411
monovalent inorganic cation transporter activity	-0.441	0	0	-4.408021	10	0.03994
electron transporter activity	-0.023	2.8000896	6	-3.1018422	7	0.04598
carrier activity	-0.289	4.0621543	8	-12.165679	20	0.023625
transferase activity	0.097	19.074923	42	-12.687227	24	0.027974
catalytic activity	0.025	53.199976	116	-48.079162	93	7.09E-05
proton-transporting two-sector ATPase complex	-0.422	0	0	-1.6880515	4	0.024764
hydrogen-translocating F-type ATPase complex	-0.422	0	0	-1.6880515	4	0.024764
inner membrane	-0.338	0.6451115	2	-4.7047745	10	0.019819
extrachromosomal circular DNA	-0.195	1.9705466	5	-4.50828	8	0.033456
extrachromosomal DNA	-0.195	1.9705466	5	-4.50828	8	0.033456
endoplasmic reticulum	-0.011	6.2680131	17	-6.5718272	10	0.049052
cytoplasm	0.049	53.881622	110	-44.500056	83	0.004815
intracellular	0.10	83.220823	174	-55.152258	107	0.002094
oxidative phosphorylation	-0.417	0	0	-1.6664665	4	0.017917
DNA replication initiation	0.626	3.7557997	6	0	0	0.001496
fatty acid oxidation	-0.822	0	0	-3.2874914	4	0.037675

sulfur amino acid metabolism	-0.589	0.2312001	1	-2.5888117	3	0.050404
DNA dependent DNA replication	0.446	5.1596519	10	-0.2508499	1	7.45E-05
response to temperature	0.256	2.4665696	4	-0.9325186	2	0.016593
response to heat	0.389	2.4665696	4	-0.5213829	1	0.045385
glycolysis	-0.161	0.8571094	2	-2.1445047	6	0.005719
glucose metabolism	-0.351	0.8571094	2	-5.4201862	11	0.000218
regulation of translation	0.004	1.3317573	4	-1.3056009	3	0.015072
nucleoside triphosphate metabolism	-0.111	1.0236657	2	-1.6880515	4	0.031704
monosaccharide catabolism	-0.161	0.8571094	2	-2.1445047	6	0.010791
alcohol catabolism	-0.161	0.8571094	2	-2.1445047	6	0.010791
glucose catabolism	-0.161	0.8571094	2	-2.1445047	6	0.010791
hexose catabolism	-0.161	0.8571094	2	-2.1445047	6	0.010791
protein-nucleus import	0.530	3.7114818	7	0	0	0.026516
amine biosynthesis	-0.338	1.0005872	2	-3.3664601	5	0.026516
monosaccharide metabolism	-0.378	0.8571094	2	-6.1543298	12	0.00071
hexose metabolism	-0.351	0.8571094	2	-5.4201862	11	0.00169
S phase of mitotic cell cycle	0.384	6.8410074	14	-0.6972074	2	0.000442
DNA replication	0.384	6.8410074	14	-0.6972074	2	0.000442
main pathways of carbohydrate metabolism	-0.256	0.8571094	2	-3.925259	10	0.003322
carbohydrate catabolism	-0.161	0.8571094	2	-2.1445047	6	0.029502
energy derivation by oxidation of organic compounds	-0.323	1.4198075	3	-6.257679	12	0.002202
DNA replication and chromosome cycle	0.378	7.1267635	15	-0.6972074	2	0.001282
energy pathways	-0.359	1.4198075	3	-7.5263925	14	0.001924
mitotic cell cycle	0.457	15.101651	28	-0.9305031	3	2.17E-05
coenzyme metabolism	-0.513	0.3028057	1	-5.4314898	9	0.034759
protein folding	0.398	4.5118926	8	-0.5365947	2	0.043069
alcohol metabolism	-0.346	1.1939183	3	-7.0708879	14	0.009441
coenzyme and prosthetic group metabolism	-0.381	1.2459281	2	-5.4314898	9	0.045605
DNA metabolism	0.386	16.863937	33	-2.1852938	5	9.41E-05
carbohydrate metabolism	-0.240	3.1254157	8	-9.1279893	17	0.003907
cell cycle	0.436	20.308961	40	-1.1459049	4	0.009025

Continues (*) and Early(A)	cell proliferation	0.393	26.171638	49	-3.7762005	8	0.008789
	cell growth and/or maintenance	0.136	53.452631	102	-31.309554	61	0.003237
	metabolism	0.096	77.803497	165	-52.569002	98	0.001322
	oxidoreductase activity	-0.336	5.211	11	-17.994	27	0.0113
	mitochondrion	-0.379	2.9873	8	-19.276	35	0.0018
	cytosol	0.312	10.557	21	-2.4344	5	0.0264
	fatty acid metabolism	-0.537	0.7428	2	-6.6505	9	0.0415
	carboxylic acid metabolism	-0.509	1.4427	4	-14.162	21	0.0093
	organic acid metabolism	-0.509	1.4427	4	-14.162	21	0.01
	biosynthesis	0.043	16.388	31	-13.952	25	0.0022
	macromolecule biosynthesis	0.134	14.8	28	-8.7637	17	0.0148
	physiological process	0.105	111.7	224	-73.559	139	0.0049

Early(A)/ Late(B)/ Continuous (*)	Category	Average Expression	Total Expression UP	No Genes UP	Total Expression DOWN	No Genes DOWN	p<0.05
Continues (*) and Early(A)	oxidoreductase activity	-0.531	4.3187	7	-20.252	23	0.0004
	mitochondrion	-0.590	1.3594	3	-16.12	22	0.0205
	cytosol	0.410	11.692	15	-3.0865	6	0.0015
	fatty acid metabolism	-0.530	1.2748	2	-8.6969	12	0.00001
	carboxylic acid metabolism	-0.608	1.8196	3	-18.231	24	4E-07
	organic acid metabolism	-0.608	1.8196	3	-18.231	24	4E-07
	biosynthesis	0.223	18.016	24	-10.207	11	0.0099
	macromolecule biosynthesis	0.413	18.016	24	-5.6193	6	0.0144
	physiological process	0.125	103.31	134	-75.551	88	0.0051
	defense response	0.696	16.7006662	24	0	0	0.039612
Continues (*) and Late(B)	response to biotic stimulus	0.581	16.7006662	24	-1.594032	2	0.033838
	response to external stimulus	0.493	21.7840142	30	-4.0365428	6	0.007599
	extracellular space	0.248	39.566685	49	-21.740572	23	0.004952
	L-phenylalanine metabolism	-1.203	0	0	-3.6084015	3	0.015458
Continuous (*)	phenylalanine catabolism	-1.203	0	0	-3.6084015	3	0.015458
	aromatic amino acid family catabolism	-1.203	0	0	-3.6084015	3	0.024874
	aromatic compound catabolism	-1.203	0	0	-3.6084015	3	0.024874

immunoglobulin binding	1.103	3.30923671	3	0	0	0.035077
cytosolic ribosome (sensu Eukarya)	0.823	9.87532021	12	0	0	2.15E-08
eukaryotic 48S initiation complex	0.749	2.9978872	4	0	0	0.007969
cytosolic small ribosomal subunit (sensu Eukarya)	0.749	2.9978872	4	0	0	0.007969
eukaryotic 43S preinitiation complex	0.688	3.43951302	5	0	0	0.005113
amino acid catabolism	-0.940	0	0	-5.639126	6	0.002465
amine catabolism	-0.940	0	0	-5.639126	6	0.003956
actin filament	0.340	2.02074983	3	-0.6610948	1	0.034693
small ribosomal subunit	0.746	3.73192432	5	0	0	0.014953
ribosome biogenesis	0.872	8.71636391	10	0	0	0.000176
ribosome biogenesis and assembly	0.872	8.71636391	10	0	0	0.000215
anion transporter activity	-0.381	0.86455186	1	-2.7709958	4	0.024795
inorganic anion transport	0.283	2.54243996	3	-1.1252084	2	0.030187
aromatic compound metabolism	-0.396	2.14211399	2	-5.3088476	6	0.003206
structural constituent of ribosome	0.799	15.9701069	20	0	0	5.05E-07
chemokine receptor binding	0.903	4.51414395	5	0	0	0.04313
G-protein-coupled receptor binding	0.903	4.51414395	5	0	0	0.04313
chemokine activity	0.903	4.51414395	5	0	0	0.04313
posttranslational membrane targeting	-0.049	2.61952085	4	-2.9596796	3	0.013421
basement membrane	0.991	4.95649472	5	0	0	0.051961
ribosome	0.786	16.5148623	21	0	0	1.5E-06
blood coagulation	0.419	4.82540533	6	-1.4758496	2	0.007437
hemostasis	0.419	4.82540533	6	-1.4758496	2	0.0095
heparin binding	0.342	3.84657601	4	-1.7921275	2	0.044879
protein-ER targeting	-0.049	2.61952085	4	-2.9596796	3	0.026414
anion transport	-0.033	2.54243996	3	-2.7709958	4	0.026414
protein-membrane targeting	-0.049	2.61952085	4	-2.9596796	3	0.026414
chemotaxis	0.845	5.91347974	7	0	0	0.038606
taxis	0.845	5.91347974	7	0	0	0.038606
ribonucleoprotein complex	0.764	19.0966734	25	0	0	1.68E-05
actin binding	0.177	4.89579982	8	-2.9470927	3	0.012932

	response to chemical substance	0.610	7.13862643	9	-1.0401916	1	0.02206	
	amino acid metabolism	-0.695	0.5447554	1	-7.4931106	9	0.025541	
	structural molecule activity	0.849	30.5748631	36	0	0	6.36E-06	
	amino acid and derivative metabolism	-0.755	0.5447554	1	-9.6036406	11	0.021417	
	response to abiotic stimulus	0.472	9.99208761	12	-2.4425107	4	0.011197	
	cytoplasm organization and biogenesis	0.736	19.5172428	23	-1.1062014	2	0.001275	
	ion transporter activity	-0.561	1.42337687	2	-8.1543369	10	0.035369	
	amine metabolism	-0.755	0.5447554	1	-9.6036406	11	0.047678	
	protein biosynthesis	0.772	16.2160128	21	0	0	0.012248	
	RNA binding	0.606	13.1020883	17	-1.5930626	2	0.019029	
	cell organization and biogenesis	0.723	21.3449184	26	-1.1062014	2	0.010322	
	extracellular	0.283	43.5375175	54	-21.740572	23	0.009792	
	<b>Ontology</b>	<b>Late (B)</b>						
Early(A)/ Late(B)/ Continuous (*)	<b>Category</b>	<b>Average Expression</b>	<b>Total Expression UP</b>	<b>No Expression UP</b>	<b>Total Expression DOWN</b>	<b>No Expression DOWN</b>	<b>p&lt;0.05</b>	<b>Enrichment</b>
Late (B)	urea cycle intermediate metabolism	0.244	1.130631	2	-0.39848	1	0.0157	14.066206
	MHC class I receptor activity	0.765	2.295813	3	0	0	0.02366	11.645783
	antigen processing\ endogenous antigen via MHC class I	0.765	2.295813	3	0	0	0.02525	11.252964
	antigen presentation\ endogenous antigen	0.765	2.295813	3	0	0	0.02525	11.252964
	collagenase activity	0.877	2.629886	3	0	0	0.0343	9.7048193
	phospholipase inhibitor activity	0.893	2.679154	3	0	0	0.0343	9.7048193
	antigen presentation	1.021	7.147112	7	0	0	4.4E-05	9.3774704
	antigen processing	1.122	6.732498	6	0	0	0.00037	8.6561265
	hydrolase activity\ acting on carbon-nitrogen (but not peptide) bonds\ in linear amides	0.518	1.55403	3	0	0	0.04642	8.3184165
	proteasome core complex (sensu Eukarya)	0.594	2.377945	4	0	0	0.03453	5.3784861



	apoptosis inhibitor activity	0.489	2.446018	5	0	0	0.03658	3.8819277
	hydrolase activity, acting on carbon-nitrogen (but not peptide) bonds	0.484	2.904975	6	0	0	0.0473	2.9860982
	immune response	0.779	27.7517	30	-2.03277	3	8.2E-07	2.5788043
	apoptosis regulator activity	0.496	3.966895	8	0	0	0.05082	2.3526835
	response to pest/pathogen/parasite	0.732	14.8756	16	-1.69189	2	0.00157	2.3281995
	response to wounding	0.395	6.433227	10	-1.69189	2	0.01308	2.3201989
	extracellular matrix	0.844	13.51148	16	0	0	0.01161	2.0214444
	transmembrane receptor activity	0.677	16.22933	21	-0.66253	2	0.01162	1.7370494
	peptidase activity	0.464	10.75818	19	-1.01553	2	0.03044	1.6304096
	response to stress	0.540	16.76545	20	-3.267	5	0.04162	1.4979985
	integral to plasma membrane	0.305	12.9202	17	-4.98278	9	0.04397	1.4742236
	receptor activity	0.516	21.37252	32	-2.26642	5	0.02041	1.4391916
	signal transducer activity	0.428	29.10036	46	-5.14292	10	0.01616	1.332034
Continues (*) and Late(B)	defense response	0.788	29.62142	32	-2.03277	3	1.3E-05	2.2027615
	response to biotic stimulus	0.743	30.79255	34	-2.57173	4	5.4E-06	2.1928854
	response to external stimulus	0.607	31.1322	35	-5.01693	8	9E-05	1.8370443
	extracellular space	0.692	53.45553	65	-4.34795	6	0.03805	1.2228305

Table 14:

The differential gene expressions clustered into 27 trends in a timely dependent fashion, three of which were singletons. For each gene, the data is presented in fold ratios from the normal genes expression across the whole RRR period, with the gene identifiers. Highlighted in gray are the pattern identification number. and gene symbol.

Table 15: Molecular drug targets found among the concordantly expressed genes.

The genes expressed concordantly between RRR and RCC were used to search for known Molecular drug targets. Listed are the concordant gene symbol, the expression in RRR and RCC relative to normal kidney, the actual gene that is targeted by the drug, is the targeted gene is a concordant gene or in its pathway, manufacturer, generic name of the drug, the world status of the drug (no development reported, discontinued, preclinical, Phase I-III Clinical Trials, launched and fully launched) and the drug therapy description.

Table 16: Molecular diagnostic markers among the discordantly expressed genes.

Out of all the discordant genes, three genes, FHIT, KDR and VEGF were reported in diagnostic immunohistochemistry of clinical samples of various pathologies. Further information is available at Linscott's Directory (<http://www.linscottsdirectory.com>) and ImmunoQuery (<http://www.immunoquery.com>).

5

**Table 21. Pathway analysis of genes differentially expressed in RRR and RCC.**

RRR+RCC All genes	RRR+RCC Concordant	RRR+RCC Discordant
VHL	VHL	VHL
Hypoxia	Hypoxia	Hypoxia
HIF (HRE)		HIF (HRE)
IGF		IGF
MYC	MYC	
p53	p53	p53
NF-κB	NF-κB	

Genes differentially expressed on both RRR and RCC were analyzed for significant enrichment ( $p < 0.05$ ) in genes belonging to VHL, hypoxia, HRE, IGF1, MYC, p53 and NF-κB pathways. The RRR genes were not filtered by phases of expression (*i.e.*, continuous, early and late; further details are given in Table 18).

**Table 22. Gene ontology analysis of concordant and discordant genes in RRR and RCC**

15

GO categories enriched in concordant or discordant genes in RRR and RCC are shown. The average  $\log_2$  change in gene expression for genes associated with each category is shown. Red and green shading indicate up- and down-regulated genes, respectively (further details are given in Table 17).

20

Table 22

Concordant expression

GO System	GO term	# Genes UP / DOWN	GO term average fold change	Category enrichment
Molecular Function	transcription factor binding	3:0		9.7
	structural constituent of ribosome	24:0		4.7
	RNA binding	27:1		2.7
	extracellular matrix structural constituent	6:0		2.1
Cellular Component	cytosolic ribosome	11:0		8.1
	cytoskeleton	4:0		5.6
	cytosolic actin complex	5:0		4.8
	extracellular matrix	13:1		1.9
	DNA replication initiation	4:0		4.8
	population of transcription	4:0	0.137	4.8
Biological Process	transcription	13:0		4.8
	translational membrane transport	5:2	1.64	3.5
	cytoplasm organelle and biosynthesis	20:2		1.6
	macromolecular transport	23:3		1.7
	cell adhesion	21:0		1.7
	transcription	7:1	0.055	1.3
	cell growth and/or maintenance	60:10		3.3
	protein-metabolism	5:2	0.045	3.9
	protein-ER targeting	33:1		1.2
	cell proliferation			

Discordant expression

GO System	GO term	# Genes UP / DOWN	GO term average fold change	Category enrichment
Molecular Function	transcription factor binding	2:2	0.008	21.8
	protein-cation transporter activity	1:1	0.008	10.2
	protein binding	4:2	0.253	10.2
	cell adhesion	9:30	0.045	1.3
Cellular Component	extracellular space	12:12	0.005	1.5
	transcription corepressor	0:3	0.007	1.1
	antibionics	3:2	0.068	3.3
Biological Process	regulation of cell growth	5:3	0.184	3.2
	cytoplasmic organelle and biosynthesis	6:4	0.105	2.4
	cytoplasmic organelle and biosynthesis	5:4	0.288	1.7
	morphogenesis	6:18		1.7
	cell growth and/or maintenance	13:20	0.127	1.3

**Table 23. Classification of discordant genes by functional category based on extensive analysis of the RRR and RCC literatures.**

Category	Regeneration	RCC	Gene Symbol
Morphogenesis	Up	Down	CRYM, CTGF, GPC3, CYR61, MYL6, TGF $\alpha$ , THBS1
	Down	Up	PR1, KDR, PD1, RTN3, VEGF, GADD45
	Up	Down	APOL1, IF, DCN, CTGF, GC, GPC3, CYR61, MMP2, PLAT, SDCI, THBS1, TAGLN2
Extracellular space	Up	Down	BCKHA, CD58, CXMC, IGFBP1, IGFBP3, KDR, KRT1, LPL, MEF1A, ENPP2, RTN3, VEGF
	Down	Up	APOL1, CTGF, IGFBP1
Metabolism	Up	Down	APOL1, CTGF, IGFBP1
	Down	Up	BCKHA, MACH, ENPP2, MTHFD1, MAT2A, SHMT2, SPTLC1, LPL, SHMT1, PTPB8, SOD2, CPT1A, ACOX1, EGLN1
Glycolysis	Up	Down	
	Down	Up	PGK1, HK1
Signal transduction	Up	Down	SAH1, RALBP1, NRIF, SMCL1, TAGLN2
	Down	Up	IGFBP1, IGFBP3, ARH, PCTK3, VEGF, CD88, FRAP1
Angiogenesis	Up	Down	CTGF, CYR61, THBS1
	Down	Up	VEGF, KDR
Transcription	Up	Down	TGF $\alpha$ , ZNF144, NRIF
	Down	Up	GRF1, NCOA1, NFKB1, USE2V1, EIF4A2, MNK2, SOD2
Transport	Up	Down	GC, SLCA1A1, APOE, SAH1, RALBP1
	Down	Up	SCP2, SLCA1A1, GJB2, ATP1B1, COMC, SLCO2A1, CPT1A, ACOX1, ARH
Proteolysis	Up	Down	IF, PLAT
	Down	Up	KRT1, MEF1A
Immune	Up	Down	
	Down	Up	CEACAM1, CD58
DNA	Up	Down	SMCL1, CTGF, IGFBP1
	Down	Up	TGF $\alpha$ , PRAP1, GADD45, FRAP1
Cell adhesion	Up	Down	THBS1, CTGF, IGFBP1, CYR61, IGFBP10
	Down	Up	PKD1
Cell differentiation	Up	Down	
	Down	Up	PHL1, GADD45
De phosphorylation	Up	Down	PTPRB, PCTK3, MNK2, KDR
	Down	Up	PTPRB, PCTK3, MNK2, KDR
Ubiquitination	Up	Down	JN144
	Down	Up	USE2V1, EGLN1
Other	Up	Down	TGF $\alpha$ , MMP2, TAGLN2, SDCI, CORO1B, WSB1, MYL6, AKAP2, CRYM, DCN
	Down	Up	NARS, C16orf3, RTN3, KIAA1049, HSPH1, KOP2A, ADD3, HSPD5, CAPN1

Table 2

Go System	Category	Early Pattern: Category Average Expression (RRR phases: I, E, early M)	Late Pattern: Category Average Expression (RRR phases: M, R)	Continues Pattern: Category Average Expression (RRR phases: I,E, M, R)	No Genes UP	No Genes DOWN
Molecular Function	ATP-binding and phosphorylation- dependent chloride channel activity	-0.477			0	3
	cyclophilin-type peptidyl-prolyl cis-trans isomerase activity	0.336			4	1
	cis-trans isomerase activity	0.170			4	2
	intramolecular isomerase activity	-0.533			1	5
	growth factor binding	-0.453			1	5
	transferase activity <sup>\</sup> , transferring alkyl or aryl (other than methyl) groups	0.031			4	3
	lyase activity	-0.218			5	10
	isomerase activity	-0.217			5	10
	hydrogen ion transporter activity	-0.441			0	10
	magnesium ion binding	-0.199			2	8
	monovalent inorganic cation transporter activity	-0.441			0	10
	carrier activity	-0.326			7	21
	oxidoreductase activity	-0.377		-0.573	9; 6	26; 22
	MHC class I receptor activity		0.767		3	0
	collagenase activity		0.877		3	0
	phospholipase inhibitor activity		0.897		3	0
	hydrolase activity <sup>\</sup> , acting on carbon- nitrogen (but not peptide) bonds <sup>\</sup> , in linear amidines		0.517		3	0
	apoptosis inhibitor activity		0.486		5	0
	immunoglobulin binding			1.103	3	0
	anion transporter activity			-0.384	1	4
	structural constituent of ribosome			0.798	20	0
	chemokine activity			0.902	5	0
	actin binding			0.176	8	3
	structural constituent of cytoskeleton			0.968	8	0
	RNA binding			0.605	17	2
Cellular Component	hydrogen-translocating F-type ATPase complex	-0.423			0	4
	mitochondrial inner membrane	-0.371			2	9
	extrachromosomal DNA	-0.194			5	8
	cytoplasm	0.059			118	84
	mitochondrion	-0.393		-0.590	8; 3	35; 22
	cytosol	0.340		0.410	21; 15	4; 6
	proteasome core complex (sensu Eukarya)		0.595		4	0
	microfibril		1.296		7	0
	extracellular space		0.664	0.247	64; 49	8; 23
	cytosolic ribosome (sensu Eukarya)			0.823	12	0

Biological Process	cytosolic small ribosomal subunit (sensu Eukarya)		0.750	4	0
	small ribosomal subunit		0.746	5	0
	actin filament		0.340	3	1
	extracellular		0.282	54	23
	oxidative phosphorylation	-0.418		0	4
	DNA replication initiation	0.692		5	0
	regulation of translation	0.003		4	3
	group transfer coenzyme metabolism	-0.452		0	5
	ribonucleoside triphosphate biosynthesis	-0.256		1	4
	purine ribonucleoside triphosphate biosynthesis	-0.256		1	4
	glycolysis	-0.163		2	6
	S phase of mitotic cell cycle	0.389		12	2
	fatty acid metabolism	-0.550	-0.523	2; 2	8; 10
	biosynthesis	0.051	0.223	30; 24	23; 11
	urea cycle intermediate metabolism		0.243	2	1
	antigen presentation <sup>1</sup> , endogenous antigen		0.767	3	0
	antigen				
	antigen processing <sup>1</sup> , endogenous antigen via MHC class I		0.767	3	0
	response to wounding		0.384	8	2
	response to pest/pathogen/parasite		0.791	13	2
	catabolism		0.526	25	3
	defense response		0.849	0.696	26; 24
	phenylalanine catabolism		-1.203	0	3
	amino acid biosynthesis		-0.873	0	4
	ribosome biogenesis		0.872	10	0
	inorganic anion transport		0.282	3	2
	aromatic compound metabolism		-0.366	2	5
	posttranslational membrane targeting		-0.049	4	3
	blood coagulation		0.340	5	2
	anion transport		-0.034	3	4
	ER organization and biogenesis		-0.049	4	3
	amino acid metabolism		-0.721	1	8
	response to chemical substance		0.564	8	1
	cytoplasm organization and biogenesis		0.543	26	5
	macromolecule biosynthesis		0.771	21	0
	protein biosynthesis		0.771	21	0
	organelle organization and biogenesis		0.387	16	5

Table 4

A. All genes changed in both renal regeneration and RCC:								
No.	Category name	Category size (No. of genes) (A)	No. of genes that are changed in renal regeneration (B)	No. of genes that are changed on both renal regeneration and RCC (C)	% of all the 361 genes changed on both renal regeneration and RCC	In a category: the % of renal regeneration genes that are changed on both renal regeneration and RCC (C/B)	% of all the category that is changed on both renal regeneration and RCC (C/A)	p value
1	RCC	984	361	361	100	100	37	<0.00001
2	VHL pathway	282	104	75	21	72	27	<0.00001
3	Hypoxia pathway	251	95	51	14	54	28	<0.00001
4	HRE target (HIF)	39	17	11	3	65	20	<0.0001
5	IGF pathway	129	37	17	5	46	12	0.0053
6	Myc pathway	368	136	65	18	48	18	<0.00001
7	p53 pathway	1259	262	112	31	43	9	<0.0001
8	NF- $\kappa$ B pathway	200	52	24	7	46	12	0.001
B. Genes changed concordantly between renal regeneration and RCC:								
No.	Category name	Category size (No. of genes) (A)	No. of genes that are changed in renal regeneration (B)	No. of genes that are changed on both renal regeneration and RCC (C)	% of all the 361 genes changed on both renal regeneration and RCC	In a category: the % of renal regeneration genes that are changed on both renal regeneration and RCC (C/B)	% of all the category that is changed on both renal regeneration and RCC (C/A)	p value
1	RCC	984	361	278	77	77	28	<0.00001A
2	VHL pathway	282	104	59	16	57	21	<0.00001
3	Hypoxia pathway	251	95	35	10	37	14	<0.0001
4	HRE target (HIF)	39	17	4	1	24	10	0.2205

5	IGF pathway	139	37	9	3	24	7	0.4614
6	Myo pathway	368	136	55	15	40	15	<0.00001
7	p53 pathway	1259	262	80	22	31	6	0.0043
8	NF- $\kappa$ B pathway	200	52	19	5	37	10	0.0027
C. Genes changed discordantly between renal regeneration and RCC:								
No.	Category name	Category size (No. of genes) (A)	No. of genes that are changed in renal regeneration (B)	No. of genes that are changed on both renal regeneration and RCC (C)	% of all the 361 genes changed on both renal regeneration and RCC	In a category: the % of renal regeneration genes that are changed on both renal regeneration and RCC (C/B)	% of all the category that is changed on both renal regeneration and RCC (C/A)	p value
1	RCC	984	361	83	23	23	8	<0.00001A
2	VHL pathway	282	104	16	5	15	6	<0.0001
3	Hypoxia pathway	251	95	16	4	17	6	<0.0001
4	HIF target (HIF)	39	17	7	2	41	18	<0.0001
5	IGF pathway	139	37	8	2	22	6	<0.0001
6	Myo pathway	368	136	10	3	7	3	0.0551
7	p53 pathway	1259	262	32	9	12	3	0.0003
8	NF- $\kappa$ B pathway	200	52	5	2	10	3	0.5217



Table 6

RRR/ RCC	RRR pattern	Early I, E, early M	Late M, R	Continues I, E, M, R
Concordance		regulation of translation		
		physiological processess		physiological processess
		biosynthesis		biosynthesis
		cytosol		cytosol
				structural molecule activity
				protein biosynthesis
				ribonucleoprotein protein
				ribosom
				structural constituent of ribosom
				macromolecule biosythesis
				cytosolic ribosome sensu Eukarya
				ribosome biogenesis and assembly
				ribosome biogenesis
				RNA binding
				cytoplasm organization and biogenesis
				cell organization and biogenesis
				smal ribosomal subunit
				eukaryotic 43S pre-initiation complex
			immunoglobulin binding	immunoglobulin binding
			defense response	defense response
			response to biotic stimulus	response to biotic stimulus
			response to external stimulus	response to external stimulus
				protein-ER targeting
				postranslational membrane targeting
				protein-membrane targeting
				ER organization and biogenesis
		DNA dependent DNA replication		
		DNA replication initiation		
		cell growth and/or maintenance		
		oranic acid metabolism		oranic acid metabolism
		carboxylic acid metabolism		carboxylic acid metabolism
Discordance		growth factor binding		
			extracellular space	organelle organization and biogenesis

Table 7

Gene Symbol
CRYM; CTGF; GPC3; CYR61; MYL6; TCF21; THBS1
FHL1; KDR; PKD1; RTN3; VEGF; GADD45G
AKAP2; MYL6; CORO1B
CD59; KIF21A; LPL; SCP2; ADD3; ARHE; MKNK2; NCOA4
AKAP2; APOE; NR2F6; CTGF; GC; CYR61; MYL6; SARI; SLC1A1; CORO1B; SMC1L1; GPC3
ATP1B1; CAPNS1; CD59; CPT1A; FHL1; IGFBP1; IGFBP3; KIF21A; LPL; PKD1; RRM1; SCP2; SLC16A7; SLC22A1; TOP3B; VEGF; ADD3; FRAP1; ARHE
NR2F6; SMC1L1
PKD1; RRM1; TOP3B; VEGF; FRAP1
FHL1; KDR; GADD45G
NR2F6; TCF21; ZNF144; SMC1L1
EIF4A2; TOP3B; NCOA4; PAPOLA; MKNK2
APOE <sup>HB</sup> ; IF; DCN; CTGF <sup>HB</sup> ; GC; GPC3; CYR61; MMP2; PLAT; SDC1; THBS1 <sup>HB</sup> ; TACSTD2
BCKDHA; CD59; COX6C; IGFBP1; IGFBP3; KDR; Kik1; LPL <sup>HB</sup> ; MEPIA; ENPP2; RTN3; VEGF <sup>HB</sup>
CTGF; CYR61; THBS1
VEGF; KDR
SMC1L1
GADD45G; FRAP1 <sup>REC</sup>
IF; MMP2; PLAT
HK1; Kik1; LPL; AMACR; MEPIA; PGK1; SHMT1; ACOX1; CPT1A; SCP2
SARI; SMC1L1 <sup>ASE</sup>
ATP1B1 <sup>ASE</sup> ; EIF4A2 <sup>ASE</sup> ; HARS; HK1; HSPH1; HSPD1; KDR; KIF21A; MKNK2; PCTK3; ARHE; MTHFD1; MAT2A
BCKDHA; COX6C; CPT1A; HSPD1; AMACR; SCP2; SOD2
CTGF; THBS1
RTN3; GADD45G <sup>HO</sup>
IF; FHIT; MMP2; PLAT; PPP2CB; PTPRO; SARI; SMC1L1
ACOX1; ATP1B1; BCKDHA; CAPNS1; COX6C; CPT1A; EIF4A2; HARS; HK1; KDR; Kik1; LPL; AMACR; MEPIA; MKNK2; PCTK3; ENPP2; PGK1; PAPOLA; PTFRB; RRM1; SCP2; SHMT1; SOD2; TOP3B; FRAP1; ARHE; MTHFD1; MAT2A
IF; SMC1L1
HSPH1; HSPD1; SOD2; GADD45G; FRAP1
IF; RALBP1; TACSTD2
GJB2; HSPH1; HSPD1; PKD1; SOD2; GADD45G
AKAP2; NR2F6; CTGF; PTPRO; RALBP1; SARI; TJP2; WSB1; IF; CYR61; THBS1; TACSTD2
KDR; PKD1; PTFRB; GADD45G; ARHE; IGFBP1; IGFBP3; VEGF; CEACAM1; GJB2
HARS; MTHFD1
IF; TACSTD2
GADD45G
ACOX1; BCKDHA; COX6C; RRM1; SOD2; MTHFD1

CTGF <sup>Δ60</sup> , FHIT, THBS1; MMP2; CYR61
RTN3 <sup>Δ60</sup> , RRM1; CEACAM1; VEGF; ENPP2; GJB2; IGFBP3; CD59
CTGF; THBS1
CEACAM1; ARHE
CTGF; CYR61; Gpc3; Taestd2
IGFBP1; IGFBP3; VEGF; Cox6c
FHIT; IF; MMP2; MT2A
CEACAM1; EIF4A2; FHL1; HSPH1; IGFBP3; MTHFD1; PCTK3; SHMT2; VEGF; CD59; EGLN1; HSPD1
MMP2 <sup>Δ60</sup>
CEACAM1; FHL1; IGFBP3 <sup>Δ60</sup> ; VEGF <sup>Δ60</sup> ; CD59 <sup>Δ60</sup> ; EGLN1 <sup>Δ60</sup> ; ATP1b1; SOD2; IGFBP1 <sup>Δ60</sup> ; GRSF1; HK1 <sup>Δ60</sup> ; ADD3; PGK1 <sup>Δ60</sup> ; PKD1; FRAP1
CTGF; THBS1
VEGF; GADD45G; GRSF1; PGK1; HSPH1; HSPD1; MAT2A; SHMT1
AKAP2; APOE; CYR61; FHIT; GPC3; MMP2; PLAT; PTPRO; RALBP1; SDC1; SLC1A1; SMC111; THBS1; TJP2; ZNF144
ADD3; ATP1B1; CAPNS1; CD59; GJB2; HK1; HSPD1; HSPH1; IGFBP3; KDR; LPL; MTHFD1; PKD1; RRM1; SOD2; TOP3b; VEGF
HSPD1; GFBP1; PGK1; SOD2; VEGF
PLAT
SOD2; IGFBP3; RRM1
FHIT; GPC3; TJP2
PKD1; RRM1
CYR61; GPC3; MMP2; NR2F6
EIF4A2; NCOA4
FHIT

Table 9

Gene name	Symbol Human	Expression of regeneration/normal : Early(A)/ Late(B)/ both (*) Vs. Normal; (Up (+); Down (-))	RCC/ Normal Kidney	RCC	Concordant (C) or Disconcordant (DC) with the current renal regeneration dataset	Hypoxia/ Normoxia
S100 calcium binding protein A10 (calpactin)	S100A10	(+)				
spermidine synthase	SRM	(+)				
S100 calcium binding protein A6 (calcyclin)	S100A6	(+)				
solute carrier family 26, member 4	SLC26A4	(-)				
ajuba	JUB	(+)				
keratin complex 1, acidic, gene 19	KRT19	(+)	(+)	RCC	C	(+)
RIKEN cD E130113K08 gene	T50835	(+)				
vascular cell adhesion molecule 1	VCAM1	(+)	(+)	RCC	C	
ectonucleoside triphosphate diphosphohydrolase 5	ENTPD5	(-)				
tuftelin 1	TUFT1	(+)				
cell division cycle 42 homolog (S. cerevisiae)	CDC42	(+)	(+)	RCC	C	(+)
WNT1 inducible siging pathway protein 1	WISP1	(+)				
cardiac responsive adriamycin protein	CARP	(+)				
procollagen, type V, alpha 2	COL5A2	(+)	(+)	RCC	C	
heat shock 70 kDa protein 4	HSPA4	(+)				
ATP-binding cassette, sub-family A (ABC1), member 7	ABCA7	(+)				
Mus musculus, Similar to hypothetical protein FLJ12618, clone MGC:28775 IMAGE:4487011, mR, complete cds	FLJ12618	(-)				
DJ (Hsp40) homolog, subfamily B, member 12	Djb12	(-)				
ribosomal protein S19	RPS19	(+)	(+)	RCC	C	
mitochondrial ribosomal protein L39	MRPL39	(-)				
tumor necrosis factor receptor superfamily, member 10b	TNFRSF10B	(+)				(+)
ATP synthase, H+ transporting mitochondrial F1 complex, beta subunit	ATP5B	(-)				
golgi autoantigen, golgin subfamily a, 4	GOLGA4	(-)				
cytochrome P450, 2d9	CYP2D6	(-)				
tight junction protein 2	TJP2	(+)	(-)	RCC	DC	
serine protease inhibitor, Kunitz type 1	SPINT1	(+)				
caspase 1	CASP1	(-)	(+/-)	RCC	conflict	

kynureninase (L-kynureninase hydrolase)	KYNU	(-)				
histidyl tR synthetase	HARS	(-)	(+)	RCC	DC	
acetyl-Coenzyme A dehydrogenase, medium chain	ACADM	(-)				
neutrophil cytosolic factor 2	NCF2	(+)				
caspase 8	CASP8	(+)				(+)
cell death-inducing D fragmentation factor, alpha subunit-like effector B	CIDEB	(-)				(+)
oncostatin receptor	OSMR	(+)				
elafin-like protein I	SWAM1	(-)				
glutathione peroxidase 1	GPX1	(+)	(+)	RCC	C	
Rhesus blood group-associated C glycoprotein	RHCG	(-)				
GPI-anchored membrane protein 1	M11S1	(+)	(+)	RCC	C	
transcription elongation factor A (SII), 3	TCEA3	(-)				(+)
arachidate 12-lipoxygenase, pseudogene 2	ALOX12P2	(-)				
expressed in non-metastatic cells 2, protein (NM23B) (nucleoside diphosphate kinase)	NME2	(+)	(+)	RCC	C	
ribosomal protein S2	RPS2	(+)	(+)	RCC	C	
neural proliferation, differentiation and control gene 1	NPDC1	(+)	(+)	RCC	C	
ribosomal protein L36	RPL36	(+)	(+)	RCC	C	
ribosomal protein S6	RPS6	(+)				
hepatoma-derived growth factor	HDGF	(+)				
DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 50 / nucleolar protein GU2	DDX50	(+)				
SEC61, gamma subunit (S. cerevisiae)	SEC61G	(+)	(+)(-)	RCC	conflict	
hypothetical protein, MNCb-5210	COBRA1	(+)				
phosphofructokinase, liver, B-type	PFKL	(-)				(+)
D segment, Chr 12, ERATO Doi 604, expressed	TSSC1	(+)				
carbonic anhydrase 5a, mitochondrial	CA5A	(-)				
secreted and transmembrane 1	SECTM1	(-)				
actin-like	ACTG1	(+)				
hyaluron mediated motility receptor (RHAMM)	HMMR	(+)				
complement component factor i	IF	(+)	(-)	RCC	DC	
carboxylesterase 3	CES3	(-)				
ESTs, Weakly similar to T29029 hypothetical protein F53G12.5 - Caenorhabditis elegans (C.elegans)	4931439A04Rik	(+)				
RIKEN cD A330103N21 gene	A330103N21Rik	(-)				
retinoblastoma binding protein 4	RBBP4	(+)				

Mus musculus, Similar to 60S ribosomal protein L30 isolog, clone MGC:6735 IMAGE:3590401, mR, complete cds		(-)				
cysteine rich protein 61	CYR61	(+)	(-)	RCC	DC	
growth arrest and D-damage-inducible 45 alpha	GADD45A	(+)				
centrin 3	CETN3	(+)				
karyopherin (importin) alpha 2	KPNA2	(+)	(+)	RCC	C	
expressed sequence AW541137	NUP107	(+)				
tumor necrosis factor receptor superfamily, member 1a	TNFRSF1A	(+)	(+)	RCC	C	
alkaline phosphatase 2, liver	ALPL	(-)	(-)	RCC	C	
thioredoxin 1	TXN	(+)	(-)/(+)	RCC	conflict	
ATPase, H+/K+ transporting, alpha polypeptide	ATP4A	(-)				
cytochrome P450, 2j5	CYP2J2	(-)				
solute carrier family 22 (organic cation transporter)-like 2	Slc22a2	(-)				
eukaryotic translation initiation factor 4A1	EIF4A1	(+)	(+)	RCC	C	
heparan sulfate 2-O-sulfotransferase 1	HS2ST1	(+)				
microtubule-associated protein tau	MAPT	(-)				
hydroxysteroid 17-beta dehydrogenase 7	HSD17B7	(-)				
dopa decarboxylase	DDC	(-)	(-)	RCC	C	
cytochrome c oxidase, subunit VIIa 1	COX7A1	(-)				
ubiquitin specific protease 2	USP2	(-)	(-)	RCC	C	
fragile histidine triad gene	FHIT	(+)	(-)	RCC	DC	
ESTs, Weakly similar to ADT1 MOUSE ADP.ATP CARRIER PROTEIN, HEART/SKELETAL MUSCLE ISOFORM T1 (M.musculus)		(-)				
ganglioside-induced differentiation-associated-protein 3	MRPS33	(+)				
sideroflexin 1	SFXN1	(-)				
SFFV proviral integration 1	SP11	(+)				
ribosomal protein L13a	RPL13A	(+)	(+)	RCC	C	
R polymerase I associated factor, 53 kD	PAF53	(+)				
Unknown		(-)				
ESTs		(+)				
expressed sequence AI450991	KIAA0729	(+)				
importin 11 (RIKEN cD 2510001A17 gene)	IPO11	(+)				
ESTs -pending	PCSK9	(+)				

SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5	SMARCA5	(+)	(+)	RCC	C	
epidermal growth factor	EGF	(-)	(-)	RCC	C	
hypothetical protein, I54	X61497	(-)				
mannose-6-phosphate receptor, cation dependent	M6PR	(+)				
urokinase plasminogen activator receptor	PLAUR	(+)	(+)	RCC	C	
ESTs		(-)				
chloride channel calcium activated 1	CLCA1	(+)				
ornithine aminotransferase	OAT	(-)				
Mus musculus, Similar to DKFZP586B0621 protein, clone MGC:38635 IMAGE:5355789, mR, complete cds	CIQTNF5	(+)				
peroxisome proliferator activated receptor alpha	PPARA	(-)				(-)
RIKEN cD 4930552N12 gene	MCCC2	(-)				
RIKEN cD 2310009E04 gene	FLJ10986	(-)				(+)
ribosomal protein L41	RPL41	(+)	(+)	RCC	C	
RAB11a, member RAS oncogene family	RAB11A	(+)	(+)	RCC	C	
apolipoprotein E	APOE	(+)	(-)	RCC	DC	
proteasome (prosome, macropain) subunit, beta type 8 (large multifunctional protease 7)	PSMB8	(+)	(+)	RCC	C	
osteomodulin	OMD	(-)				
cytochrome c oxidase, subunit VIIIa	COX8	(-)				
RIKEN cD 2010012D11 gene	2010012D11Rik	(-)				
EGL nine homolog 1 (C. elegans)	EGLN1	(-)	(+)	RCC	DC	(+)
DI (Hsp40) homolog, subfamily C, member 5	DNAJC5	(+)				(+)
stearyl-Coenzyme A desaturase 1	SCD	(-)				(+)
guanine nucleotide binding protein (G protein), gamma 5 subunit	GNG5	(-)				
hydroxysteroid dehydrogenase-1, delta<5>-3-beta	HSD3B2	(-)				
bone morphogenetic protein receptor, type 1A	BMPRI1A	(+)				
expressed sequence AI447451	AI447451	(+)				
CEA-related cell adhesion molecule 1	CEACAM1	(-)	(+)	RCC	DC	(+)
lactate dehydrogenase 1, A chain	LDHA	(+)	(+)	RCC	C	(+)
cold shock domain protein A	CSDA	(+)	(+)	RCC	C	
early development regulator 2 (homolog of polyhomeotic 2)	EDR2	(+)				

a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 1	ADAMTS1	(+)				
ribosomal protein L27a	RPL27A	(+)	(+)	RCC	C	(+)
ribosomal protein, large P2	RPLP2	(+)	(+)	RCC	C	
solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 7	SLC7A7	(-)	(-)	RCC	C	
acetyl-Coenzyme A acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (D18Erd240e) RIKEN cD 0610011L04 gene	ACAA2	(-)				
regulator of G-protein sigling 14	RGS14	(+)				
thymosin, beta 4, X chromosome	TMSB4X	(+)	(+)		C	(+)
metallothionein 2	MT2A	(+)	(-)	RCC	DC	
serum amyloid A 3	SAA3P	(+)				
2'-5' oligoadenylate synthetase 1A	OAS1	(+)				
chemokine (C-C) receptor 5	CCR5	(+)				
neurotrophin guanine nucleotide exchange factor	NGEF	(-)				
f-box only protein 3	FBXO3	(-)				
protein phosphatase 1, regulatory (inhibitor) subunit 1A	PPP1R1A	(-)				
phorbol-12-myristate-13-acetate-induced protein 1	PMAIP1	(+)				
NIMA (never in mitosis gene a)-related expressed kase 6	NEK6	(+)				(+)
transmembrane protein 8 (five membrane-spanning domains)	TMEM8	(-)				
kallikrein 26	Klk26	(-)				
protein tyrosine phosphatase, receptor type, C	PTPRC	(+)				
heat-responsive protein 12	UK114	(-)	(-)	RCC	C	
platelet derived growth factor, B polypeptide	PDGFB	(+)	(+)	RCC	C	
RIKEN cD 1500026A19 gene	ALG5	(+)				
transforming growth factor, beta induced, 68 kDa	TGFBI	(+)	(+)	RCC	C	(+)
baculoviral IAP repeat-containing 3	BIRC3	(+)	(+)	RCC	C	
small inducible cytokine A2	SCYA2	(+)				
endothelin 1	EDN1	(+)				(+)
dimethylarginine dimethylaminohydrolase 2	DDAH2	(+)				
phospholipid scramblase 1	PLSCR1	(+)	(+)	RCC	C	
translin	TSN	(+)				
inhibitor of D binding 2	ID2	(+)	(+)	RCC	C	
reduced expression 3	BEX1	(-)				
ribosomal protein S3	RPS3	(+)	(+)	RCC	C	(+)
cytochrome P450, 2A4	CYP2A13	(-)				



MYB binding protein (P160) 1a	MYBBP1A	(+)				
RIKEN cD 9530089B04 gene	9530089B04Rik	(-)				
malic enzyme, supertant	ME1	(-)				
ribosomal protein L44	RPL36A	(+)				
laminin B1 subunit 1	LAMB1	(+)				
hemopoietic cell phosphatase	PTPN6	(+)	(+)	RCC	C	
annexin A1	ANXA1	(+)	(+)(???)	RCC	conflict	
RIKEN cD 1110038J12 gene		(-)				
mini chromosome maintenance deficient 4 homolog (S. cerevisiae)	MCM4	(+)	(+)	RCC	C	(+)
benzodiazepine receptor, peripheral	BZRP	(+)				
solute carrier family 22 (organic cation transporter), member 1-like	SLC22A1L	(-)	(-)(+)	RCC	conflict	
karyopherin (importin) beta 3	KPNB3	(+)				
lipoprotein lipase	LPL	(-)	(+)	RCC	DC	
ATP-binding cassette, sub-family D (ALD), member 3	ABCD3	(-)				
Mus musculus, Similar to RAS p21 protein activator, clone MGC:7759 IMAGE:3498774, mR, complete cds	LOC218397	(+)				
UDP-Gal:betaGlc beta 1,3-galactosyltransferase, polypeptide 3	B3GALT3	(-)				
RIKEN cD 5031422I09 gene	PKP4	(-)				
Mus musculus, basic transcription factor 3, clone MGC:6799 IMAGE:2648048, mR, complete cds	LOC218490	(+)				
tumor-associated calcium sigl transducer 2	TACSTD2	(+)	(-)	RCC	DC	
FK506 binding protein 5 (51 kDa)	FKBP5	(-)				
endoplasmic reticulum protein 29	C12orf8	(+)				
plasminogen activator, tissue	PLAT	(+)	(-)	RCC	DC	
ribosomal protein S29	RPS29	(+)				
cytochrome P450, family 4, subfamily v, polypeptide 3 / expressed sequence AW111961	Cyp4v3	(+)				
CEA-related cell adhesion molecule 2	Ceacam2	(-)				
downstream of tyrosine kase 1	DOK1	(+)				
interleukin 11 receptor, alpha chain 1	IL11RA	(-)				
protein phosphatase 3, catalytic subunit, gamma isoform	PPP3CC	(-)				
granulin	GRN	(+)	(+)	RCC	C	
cathepsin Z	CTSZ	(+)				

protease (prosome, macropain) 26S subunit, ATPase 1	PSMC1	(+)				
expressed sequence AW047581	AW047581	(+)				
Mus musculus adult male kidney cD, RIKEN full-length enriched library, clone:0610012C11:homogenisato 1, 2-dioxygese, full insert sequence		(-)				
RIKEN cD 5730403B10 gene	C16orf5	(-)	(+)	RCC	DC	
ESTs, Weakly similar to simple repeat sequence-containing transcript (Mus musculus) (M.musculus)		(+)				
T-cell specific GTPase	Tgtp	(+)				
CD68 antigen	CD68	(+)	(+)	RCC	C	
transmembrane 7 superfamily member 1	TM7SF1	(-)				
mitogen activated protein kinase kinase 1	MAP3K1	(+)				
retinoblastoma binding protein 7	RBBP7	(+)	(+)	RCC	C	
small inducible cytokine A7	SCYA7	(+)				
cyclin E1	CCNE1	(+)	(+)	RCC	C	
coagulation factor II (thrombin) receptor-like 1	F2RL1	(+)				
annexin A5	ANXA5	(+)				
Unknown	ITGA5	(+)				
beta-2 microglobulin	B2M	(+)	(+)	RCC	C	(+)
eukaryotic translation initiation factor 4A2	EIF4A2	(-)	(+)	RCC	DC	
histocompatibility 2, class II, locus DMA	HLA-DMA	(+)				
ribosomal protein L35	RPL35	(+)				
expressed sequence AW413625	FLJ22794	(+)				
deltex 1 homolog (Drosophila)	DTX1	(-)	(-)	RCC	C	
kinesin family member 1B (expressed sequence AJ448212)	KIF1B	(+)				
transcription factor 21	TCF21	(+)	(-)	RCC	DC	
nuclear receptor subfamily 2, group F, member 2	NR2F2	(+)	(+)	RCC	C	
R polymerase II 1	POLR2A	(-)				
actin, alpha 2, smooth muscle, aorta	ACTA2	(+)				
neural precursor cell expressed, developmentally down-regulated gene 4a	NEDD4	(-)				
actin, gamma 2, smooth muscle, enteric	ACTG2	(+)				
mini chromosome maintenance deficient 2 (S. cerevisiae)	MCM2	(+)	(+)	RCC	C	
integrin-associated protein	CD47	(+)	(+)?	RCC	conflict	
creatine kinase, brain	CKB	(-)				(+)
3-phosphoglycerate dehydrogenase	PHGDH	(+)	(-)(+)	RCC	conflict	

ESTs, Weakly similar to 2022314A granule cell marker protein (M.musculus)		(+)				
TAF9 R polymerase II, TATA box binding protein (TBP)-associated factor, 32 kDa	TAF9	(+)				
Rai-interacting protein 1	RAIBP1	(+)	(-)	RCC	DC	
tubulin, beta 5	TUBB	(+)	(+)	RCC	C	
speckle-type POZ protein	SPOP	(-)				
amelogenin	AMELX	(+)				
tropomyosin 3, gamma	TPM3	(+)				
solute carrier family 22 (organic cation transporters), member 2	SLC22A2	(-)				
CD48 antigen	CD48	(+)				
RIKEN cD 1200014103 gene	F13A1	(+)				
avian reticuloendotheliosis viral (v-rel) oncogene related B	RELB	(+)				
growth factor receptor bound protein 7	GRB7	(-)	(-)	RCC	C	
histocompatibility 2, class II antigen A, alpha	HLA-DQA1	(+)				
proteasome (prosome, macropain) 26S subunit, non-ATPase, 10	PSMD10	(+)				
hematological and neurological expressed sequence 1	HN1	(+)	(+)	RCC	C	
heat shock protein 1 (chaperonin) / heat shock protein, 60 kDa	HSPD1	(-)	(+)	RCC	DC	
sterol carrier protein 2, liver	SCP2	(-)	(+)	RCC	DC	
RIKEN cD 1110054A24 gene	1110054A24Rik	(+)				
crystallin, alpha B	CRYAB	(+)	(+)	RCC	C	
RIKEN cD 2410026K10 gene	CD99	(+)				(+)
adenine phosphoribosyl transferase	APRT	(+)				
lectin, galactose binding, soluble 4	LGALS4	(-)				
Arpc2	ARPC2	(+)				
RIKEN cD 2600015J22 gene		(+)				
heme oxygenase (decycling) 1	HMOX1	(+)				(+)
ubiquitin-conjugating enzyme E2D 2	UBE2D2	(+)				
ubiquitin-conjugating enzyme E2H	UBE2H	(+)	(+)	RCC	C	(+)
glucose-6-phosphatase, catalytic	G6PC	(-)				
Rap1, GTPase-activating protein 1	RAP1GA1	(-)	(-)	RCC	C	
lectin, galactose binding, soluble 9	LGALS9	(+)	(+)/(-) ???	RCC	conflict	
dihydropyrimidine-like 3	DPYSL3	(+)	(+)	RCC	C	
bisphosphate 3'-nucleotidase 1	BFNT1	(-)				
connective tissue growth factor	CTGF	(+)	(-)	RCC	DC	
procollagen, type IV, alpha 2	COL4A2	(+)	(+)	RCC	C	

RIKEN cD 0610007L01 gene	FLJ10099	(+)				
cytidine 5'-triphosphate synthase	CTPS	(+)				
RIKEN cD 4430402G14 gene	H3Bb	(+)				
mutS homolog 6 (E. coli)	MSH6	(+)				
CDC16 (cell division cycle 16 homolog (S. cerevisiae))	CDC16	(+)	(+)	RCC	C	
RIKEN cD 5730534O06 gene	KIAA0164	(-)				
RIKEN cD 2610524G07 gene		(-)				
proteasome (prosome, macropain) subunit, alpha type 2	PSMA2	(+)				
solute carrier family 3, member 1	SLC3A1	(-)	(-)	RCC	C	
RIKEN cD 2310051E17 gene	2310051E17Rik	(-)				
lyric (D8Bwg1112e) D segment, Chr 8, Brigham & Women's Genetics 1112 expressed	LYRIC	(+)				
tescin XB	TNXB	(-)				
Yamaguchi sarcoma viral (v-yes-1) oncogene homolog	LYN	(+)	(+)	RCC	C	
cytochrome P450, subfamily IV B, polypeptide 1	CYP4B1	(-)				
microtubule-associated protein, RP/EB family, member 1	MAPRE1	(+)				
heat shock protein, 86 kDa 1	HSPCA	(+)	(?)	RCC	conflict	
pyruvate decarboxylase	PC	(-)				
oxysterol binding protein-like 1A	OSBPL1A	(-)				
carnitine palmitoyltransferase 1, liver	CPT1A	(-)	(+)	RCC	DC	
UDP-N-acetyl-alpha-D-galactosamine:(N-acetylneuraminy)-galactosylglucosylceramide-beta-1, 4-N-acetylgalactosaminyltransferase	GALGT	(+)				
zinc finger protein 36, C3H type-like 1	ZFP36L1	(+)	(+)	RCC	C	(+)
acyl-Coenzyme A dehydrogenase, very long chain	ACADVL	(-)				
aminooxidate-semialdehyde synthase/ (Lonsdh) lysine oxoglutarate reductase, saccharopine dehydrogenase	AASS	(-)				
RIKEN cD 1110014C03 gene	TMP21	(+)				
FXVD domain-containing ion transport regulator 5	FXVD5	(+)				
expressed sequence A1316828	FLJ20618	(+)				
phosphoglycerate kinase 1	PGK1	(-)	(+)	RCC	DC	(+)
Unknown		(+)				
RIKEN cD 1700008H23 gene	1700008H23Rik	(-)				
RIKEN cD 2810047L02 gene	RAMP	(+)				
mini chromosome maintenance deficient 7 (S. cerevisiae)	MCM7	(+)	(+)	RCC	C	

RIKEN cD 2410174K12 gene	SUGT1	(+)				
polypyrimidine tract binding protein 1	PTBP1	(+)	(+)	RCC	C	(+)
complement component 3	C3	(+)				
succinate-Coenzyme A ligase, ADP-forming, beta subunit	SUCLA2	(-)				
thioredoxin-like (32kD)	TXNL	(+)				
methionine aminopeptidase 2	METAP2	(+)				
hepsin	HPN	(-)	(-)	RCC	C	
T-cell, immune regulator 1	TCIRG1	(+)				
prothymosin alpha	PIMA	(+)	(+)	RCC	C	
RIKEN cD 0610006F02 gene	DKFZP566H073	(-)				
solute carrier family 13 (sodium/sulphate symporters), member 1	SLC13A1	(+)				
Mus musculus, clone IMAGE:3494258, mR, partial cds		(+)				
matrix gamma-carboxyglutamate (gla) protein	MGP	(+)				
leucocyte specific transcript 1	LY117	(+)	(+)	RCC	C	
Mus musculus, Similar to hypothetical protein FLJ21634, clone MGC:19374 IMAGE:2631696, mR, complete cds	FLJ21634	(-)				
complement factor H related protein 3A4/SG4	HF1	(+)				
RIKEN cD 2610200M23 gene	SSBP3	(+)	(+)	RCC	C	
(Prlr-rs1) prolactin receptor related sequence 1	PRLR	(-)				
sig1 transducer and activator of transcription 3	STAT3	(+)	(+)	RCC	C	
peptidylprolyl isomerase (cyclophilin)-like 1	PPIL1	(+)	(+)	RCC	C	
histocompatibility 2, L region	H2-L	(+)				
eukaryotic translation initiation factor 2A	eIF2a	(+)				
serine/arginine repetitive matrix 1	RAD23B	(+)				
solute carrier family 31, member 1	SLC31A1	(-)				
clusterin	CLU	(+)	(?)	RCC	conflict	
yolk sac gene 2	DKFZp761A051.1	(-)				
tubulin alpha 1	TUBA1	(+)				
guanine nucleotide binding protein, alpha inhibiting 2	GNAI2	(+)	(+)	RCC	C	
Unknown		(+)				
selenium binding protein 2	SELENBP1	(-)	(-)	RCC	C	
group specific component	GC	(+)	(-)	RCC	DC	
hexokise 1	HK1	(-)	(+)	RCC	DC	(+)
eukaryotic translation initiation factor 5A	EIF5A	(+)				

glycoprotein 49 A	Gp49a	(+)				
CDK2 (cyclin-dependent kinase 2)-associated protein 1	CDK2AP1	(+)				
core promoter element binding protein	COPEB	(+)	(+)	RCC	C	
B-cell leukemia/lymphoma 2 related protein A1b	BCL2A1	(+)				
RIKEN cD 5430416A05 gene	AD034	(+)				
protein phosphatase 1, catalytic subunit, alpha isoform	PPP1CA	(+)				
calreticulin	CALR	(+)	(-)/(+)	RCC	conflict	
RAS-related C3 botulinum substrate 2	RAC2	(+)				
glutathione S-transferase, alpha 2 (Yc2)	GSTA2	(-)	(+)(-)	RCC	conflict	
tubulin alpha 2	TUBA2	(+)				
lysosomal-associated protein transmembrane 4B	LAPTM4B	(+)				
Mitogen activated protein kinase 1; RIKEN cD 9030612K14 gene	MAPK1	(-)				(+) but blocked HIF-1 activation by hypoxia
X (tissue)-specific transcript, antisense	TSIX	(+)				
expressed sequence C80913	C80913	(+)				
Kruppel-like factor 9	BTFB1	(-)				
arachidate 5-lipoxygenase activating protein	ALOX5AP	(+)	(+)	RCC	C	
decorin	DCN	(+)	(-)	RCC	DC	
Mus musculus, Similar to Protein P3, clone MGC:38638 IMAGE:5355849, mR, complete cds	DXS253E	(+)				
matrix metalloproteinase 14 (membrane-inserted)	MMP14	(+)	(+)	RCC	C	
expressed sequence AA672638	AA672638	(-)				
RIKEN cD A230106A15 gene	A230106A15Rik	(-)				
expressed sequence AA589392	AA589392	(+)				
expressed sequence AI838057	AI838057	(-)				
transgelin	TAGLN	(+)				
LIM and SH3 protein 1	LASPI	(+)				
expressed sequence AI843960	RBPSUH	(+)				
Mus musculus, clone IMAGE:4952483, mR, partial cds	TOR2A	(+)				
RIKEN cD 2410129E14 gene		(+)				
((AW146109) expressed sequence AW146109)	CD44	(+)	(+)		C	
D-amino acid oxidase	DAO	(-)				
expressed sequence AI593524	DKFZp586A011.1	(-)				

expressed sequence AI607846	AIF1	(+)				
RIKEN cD 1190006C12 gene	SEC61B	(+)				
mannose receptor, C type 1	MRC1	(+)				
phospholipase A2, group 1B, pancreas	PLA2G1B	(+)				
adenylate cyclase 4	ADCY4	(-)				
aquaporin 2	AQP2	(-)				
expressed sequence AI182284	AI182284	(-)				
baculoviral IAP repeat-containing 2	BIRC2	(+)	(+)	RCC	C	
malonyl-CoA decarboxylase	MLYCD	(-)				
Muf1 protein (D630045E04Rik) Mus musculus, clone IMAGE:3491421, mR, partial cds	MUF1	(+)				
RIKEN cD 2610007A16 gene	SEC13L	(-)				
selenophosphate synthetase 2	SPS2	(-)	(-)	RCC	C	
apurinic/pyrimidinic endonuclease	APEX1	(+)				(+)
MAD homolog 5 (Drosophila) / expressed sequence AI451355	MADH5	(+)	(+)	RCC	C	
dipeptidase 1 (rel)	DPEP1	(-)	(-)	RCC	C	
expressed sequence AI132321	AI132321	(+)				
expressed sequence AI159688	AI159688	(-)				
gamma-glutamyl hydrolase	GGH	(+)	(+)/(-)	RCC	conflict	
Mus musculus, Similar to hypothetical protein FLJ20234, clone MGC:37525 IMAGE:4986113, mR, complete cds	FLJ20234	(+)				
expressed sequence AL022757	5730453116Rik	(+)				
Mus musculus, clone MGC:38798 IMAGE:5359803, mR, complete cds	MGC38798	(-)				
Mus musculus, Similar to cortactin isoform B, clone MGC:18474 IMAGE:3981559, mR, complete cds	EMS1	(+)				
Mus musculus, clone MGC:18985 IMAGE:4011674, mR, complete cds	FLJ20303	(+)	(+)	RCC	C	
Mus musculus, Similar to hypothetical protein FLJ10520, clone MGC:27888 IMAGE:3497792, mR, complete cds	FLJ10520	(-)				
pyridoxal (pyridoxine, vitamin B6) kinase	PDXK	(+)				
Mus musculus mR for 67 kDa polymerase-associated factor PAF67 (pat67 gene)	EIF3S61P	(+)				
cytidine 5'-triphosphate synthase 2	CTPS2	(+)				
Unknown		(+)				

epithelial membrane protein 3	EMP3	(+)	(+)	RCC	C	
ceroid-lipofuscinosis, neurol 2	CLN2	(-)				
solute carrier family 22 (organic anion transporter), member 8 / (Roc) reduced in osteosclerosis transporter	SLC22A8	(-)	(-)	RCC	C	
erythrocyte protein band 4.1-like 1	EPB41L1	(-)				
low density lipoprotein receptor-related protein 6	LRP6	(-)				
trinucleotide repeat containing 11 (THR-associated protein, 230 kDa subunit)	TNRC11	(+)				
src homology 2 domain-containing transforming protein D	SHD	(-)				(+)
ribosomal protein S6 kise, 90kD, polypeptide 4	RPS6KA4	(+)				
topoisomerase (D) III beta	TOP3B	(-)	(+)	RCC	DC	
G1 to phase transition 1	GSPT1	(+)				
transforming growth factor beta 1 induced transcript 4	TSC22	(+)	(+)	RCC	C	
mitsugumin 29	Mg29	(-)				
FK506 binding protein 9	FKBP9	(+)				
regulator of G-protein sigling 19 interacting protein 1	RGS19IP1	(+)				
transcobalamin 2	TCN2	(-)	(-)	RCC	C	
thioesterase, adipose associated	THEA	(-)				
lysyl oxidase-like	LOXL1	(+)				
nuclease sensitive element binding protein 1	NSEP1	(+)	(+)	RCC	C	
transthyretin	TTR	(-)				
RIKEN cD 5630401J11 gene	5630401J11Rik	(+)				
LPS-induced TNF-alpha factor	LITAF	(+)				
FK506 binding protein 12-rapamycin associated protein 1	FRAP1	(-)	(+)	RCC	DC	Frap1 amplified HIF signaling
interferon activated gene 204	Ifi204	(+)				
insulin-like growth factor binding protein 1	IGFBP1	(-)	(+)	RCC	DC	(+)
myeloid differentiation primary response gene 88	MYD88	(+)				
Mus musculus, similar to heterogeneous nuclear ribonucleoprotein A3 (H. sapiens), clone MGC:37309 IMAGE:4975085, mR, complete cds	MGC37309	(+)				
elastase 1, pancreatic	ELA1	(-)				
craniofacial development protein 1	CFDP1	(+)				
folate receptor 1 (adult)	FOLR1	(-)	(-)/(+)	RCC	conflict	



proteasome (prosome, macropain) 28 subunit, 3	PSME3	(-)				
TAF10 R polymerase II, TATA box binding protein (TBP)-associated factor, 30 kDa	TAF10	(+)				
E-vasodilator stimulated phosphoprotein	EVL	(+)	(+)	RCC	C	
EST AI181838	MGC2555	(-)				
cathepsin D	CTSD	(+)	(+)	RCC	C	(+)
opioid growth factor receptor	OGFR	(+)				
chloride channel, nucleotide- sensitive, 1A	CLNS1A	(+)				
Mus musculus, Similar to retinol dehydrogenase type 6, clone MGC:25965 IMAGE:4239862, mR, complete cds	RODH-4	(-)				
actin, alpha 1, skeletal muscle	ACTA1	(+)				
cytochrome c oxidase, subunit VIIa 3	COX7A3	(-)				
expressed sequence C85457	C85457	(-)				
H2B histone family, member S	H2BFS	(-)				
Mus musculus, similar to quinone reductase-like protein, clone IMAGE:4972406, mR, partial cds	VAT1	(-)				
ESTs, Weakly similar to S26689 hypothetical protein hc1 - mouse (M.musculus)		(-)				
reticulin 3	RTN3	(-)	(+)	RCC	DC	
striatin, calmodulin binding protein 4 / expressed sequence C80611	STRN4	(+)				
ESTs		(-)				
Mus musculus, similar to R29893-1, clone MGC:37808 IMAGE:5098192, mR, complete cds		(-)				
RIKEN cD 3110001N18 gene	RPL22	(+)	(+)	RCC	C	(+)
proteasome (prosome, macropain) subunit, alpha type 7	PSMA7	(+)	(+)	RCC	C	
cytochrome P450, 2c1, ethanol inducible	CYP2E1	(-)				
small nuclear ribonucleoprotein polypeptide G	SNRPG	(+)				
calponin 2	CNN2	(+)				
RIKEN cD 1200014D15 gene	DMGDH	(-)				
ESTs, Weakly similar to TYROSINE-PROTEIN KISE JAK3 (M.musculus)		(-)				
lymphocyte specific 1	LSP1	(+)	(+)	RCC	C	
RIKEN cD 4930542G03 gene	4930542G03Rik	(+)				
ESTs		(+)				

splicing factor, arginine/serine-rich 2 (SC-35)	SFRS2	(+)	(+)	RCC	C	
peroxisomal membrane protein 2, 22 kDa	PXMP2	(-)	(+)(-)	RCC	conflict	
ESTs, Moderately similar to S12207 hypothetical protein (M.musculus)		(-)				
Unknown		(-)				
CD2-associated protein	CD2AP	(+)	(+)	RCC	C	
expressed sequence AI182282	SLC9A8	(-)				
vascular endothelial zinc finger 1; expressed sequence AI848691	Vczf1	(-)				
RIKEN cD 1810038D15 gene	DKFZP566E144	(+)				
ESTs		(-)				
solute carrier family 34 (sodium phosphate), member 1	SLC34A1	(-)				
phosphoglycerate mutase 2	PGAM2	(-)				
metallothionein 1	MT1A	(+)				
Mus musculus, clone IMAGE:4974221, mRNA, partial cds	APEH	(-)	(-)	RCC	C	
histone 2, H2aa1/(Hist2) histone gene complex 2	HIST2H2AA	(-)				
epidermal growth factor-containing fibulin-like extracellular matrix protein 1	EFEMP1	(+)				
betaine-homocysteine methyltransferase	BHMT	(-)	(-)	RCC	C	
junction plakoglobin	JUP	(-)	(-)	RCC	C	
hepatic nuclear factor 4	HNF4A	(-)				Hnf4 interact with HIF1a & ARNT
expressed sequence AI194696	HFL1	(+)				
Mus musculus, clone MGC:7898 IMAGE:3582717, mRNA, complete cds		(-)				
RIKEN cD 2700038K18 gene		(+)				
Fc receptor, IgG, low affinity III	FCGR3A	(+)	(+)	RCC	C	
succinate dehydrogenase complex, subunit A, flavoprotein (Fp)	SDHA	(-)				
interleukin 1 beta	IL1B	(+)	(?)	RCC	conflict	
RIKEN cD 2700027J02 gene	SPF45	(+)				
selectin, platelet (p-selectin) ligand	SELPLG	(+)	(+)	RCC	C	
RIKEN cD 1200009B18 gene	LOC51290	(+)				
proteoglycan, secretory granule	PRG1	(+)	(+)	RCC	C	
transformation related protein 53	TP53	(+)	(+)(-??)	RCC	conflict	(+)
carboxypeptidase X 1 (M14 family) / metallocarboxypeptidase 1	CPXM	(+)				

SH3 domain binding glutamic acid-rich protein-like 3	SH3BGR13	(+)				(+)
insulin-like growth factor binding protein 4	IGFBP4	(-)				
exportin 1, CRM1 homolog (yeast)	XPO1	(+)	(+)	RCC	C	
Mus musculus, clone MGC:38363 IMAGE:5344986, mR, complete cds	TM4SF3	(+)	(-)	RCC	DC	
RIKEN cD 2310046G15 gene	SPUVE	(+)	(+)	RCC	C	
ribosomal protein L29	RPL29	(+)	(+)	RCC	C	(+)
E26 avian leukemia oncogene 2, 3' domain	ETS2	(+)				
Mus musculus, Similar to hypothetical protein FLJ13213, clone MGC:28555 IMAGE:4206928, mR, complete cds	FLJ13213	(+)				
eukaryotic translation initiation factor 3	EIF3S10	(+)				
Mus musculus, Similar to hypothetical protein DKFZp566A1524, clone MGC:18989 IMAGE:4012217, mR, complete cds	DKFZp566A1524	(+)				
RIKEN cD 1300013G12 gene	1300013G12Rik	(+)				(+)
chloride intracellular channel 4 (mitochondrial)	CLIC4	(+)				
activator of S phase kinase	ASK	(+)				
ketohexokinase	KHK	(-)	(-)	RCC	C	
expressed sequence AI265322	AI265322	(-)				
glypican 3	GPC3	(+)	(-)	RCC	DC	
EGF-like module containing, mucin-like, hormone receptor-like sequence 1	EMR1	(+)				
diaphorase 1 (DH)	DIA1	(+)				
histocompatibility 2, class II antigen E beta	H2-Eb1	(+)				
melanoma antigen, family D, 2	MAGED2	(+)				
serine/threonine kinase receptor associated protein	UNRIP	(+)				
annexin A6	ANXA6	(+)				
procollagen, type I, alpha 1	COL1A1	(+)	(+)(-?)	RCC	conflict	
Mus musculus, Similar to transgelin 2, clone MGC:6300 IMAGE:2654381, mR, complete cds	TAGLN2	(+)	(+)	RCC	C	
RIKEN cD 2810409H07 gene	PTD004	(+)				
transformed mouse 3T3 cell double minute 2	MDM2	(+)	(+)	RCC	C	
Fe receptor, IgF, high affinity I, gamma polypeptide	FCER1G	(+)	(+)	RCC	C	
selenoprotein P, plasma, 1	SEPP1	(-)	(-)	RCC	C	

serine (or cysteine) protease inhibitor, clade H (heat shock protein 47), member 1	SERPINH1	(+)				
small inducible cytokine A9	OCL9	(+)				
phospholipase A2, activating protein	PLAA	(+)				
FXD domain-containing ion transport regulator 2	FXD2	(-)	(-)	RCC	C	
cord-bleu; ESTs, Moderately similar to T00381 KIAA0633 protein (H.sapiens)	COBL	(+)				
expressed sequence AW488255	EFNB1	(-)				
Mus musculus, clone IMAGE:4486265, mR, partial cds		(+)				
protein kase C, delta	PRKCD	(+)	(+)	RCC	C	
RIKEN cD Z310067B10 gene	KIAA0195	(-)				
RIKEN cD 913001J04 gene	913001J04Rik	(+)				
RIKEN cD 3230402E02 gene	FLJ10983	(+)	(+)	RCC	C	
macrophage migration inhibitory factor	MIF	(-)				
RIKEN cD 0610041E09 gene	AD-020	(+)				
glutamine synthetase	GLUL	(-)				
prohibitin	PHB	(-)				
RIKEN cD 6330583M11 gene	DKFZP434P106	(+)	(+)	RCC	C	
tumor protein p53 binding protein, 2 / expressed sequence AI746547	TP53BP2	(-)				
expressed sequence AI315037	AI315037	(-)				
nestin -pendin	NES	(+)				
nuclear receptor subfamily 2, group F, member 6	NR2F6	(+)	(-)	RCC	DC	
Mus musculus, clone IMAGE:3994696, mR, partial cds	YUP8H12R.13	(+)				
golgi reassembly stacking protein 2	GORASP2	(+)	(+)	RCC	C	
low density lipoprotein receptor-related protein 2	LRP2	(-)	(-)	RCC	C	
ESTs, Weakly similar to YAE6-YEAST HYPOTHETICAL 13.4 KD PROTEIN IN ACS1-GCV3 INTERGENIC REGION (S.cerevisiae)		(-)				
Cbp/p300-interacting transactivator with Glu/Asp-rich carboxy-terminal domain 1	CITED1	(-)				
platelet factor 4	PF4	(+)				
ESTs		(+)				
expressed sequence AI553555	AI553555	(-)				
tumour killer tumour recognition sequence	NKTR	(+)				

expressed sequence AU019833	Clorf24	(+)				
guanylate nucleotide binding protein 2	GBP2	(+)	(+)	RCC	C	
RIKEN cD 2310004L02 gene	FLJ10241	(-)				
ESTs		(-)				
expressed sequence C79732	C79732	(-)				
Ras-GTPase-activating protein (GAP<120>) SH3-domain binding protein 2	G3BP2	(+)				
glutathione S-transferase, theta 2	GSTT2	(-)	(-)	RCC	C	
CD52 antigen	CDW52	(+)	(+)	RCC	C	
RIKEN cD 2810004N23 gene	2810004N23Rik	(+)				
ESTs	Rin3	(+)				
ESTs		(+)				
zinc finger protein 144	ZNF144	(+)	(-)	RCC	DC	
branched chain aminotransferase 2, mitochondrial	BCAT2	(-)				
phenylalanine hydroxylase	PAH	(-)	(-)	RCC	C	
ESTs, Highly similar to T00268 hypothetical protein KIAA0597 (H.sapiens)	KIAA0597	(-)				
expressed sequence AV046379	AV046379	(-)				
ribosomal protein L10A	RPL10A	(+)	(+)	RCC	C	
RIKEN cD 2410021P16 gene	MGC5601	(-)				
RIKEN cD 4632401C08 gene	4632401C08Rik	(-)				
BCL2-antagonist/killer 1	BAK1	(+)				
myelocytomatosis oncogene	MYC	(+)	(+)	RCC	C	
guanosine diphosphate (GDP) dissociation inhibitor 3	GDI-2	(+)				
enoyl Coenzyme A hydratase, short chain, 1, mitochondrial	ECHS1	(-)				
actin related protein 2/3 complex, subunit 3 (21 kDa)	ARPC3	(+)	(+)	RCC	C	(+)
retinol binding protein 1, cellular	RBP1	(+)				
solute carrier family 25 (mitochondrial carrier)	SLC25A13	(-)				
RIKEN cD 1100001F19 gene	UBE2D3	(+)				
constitutive photomorphogenic protein 1 (Arabidopsis)	COP1	(+)				
ESTs, Weakly similar to AF182426 1 arylacetamide deacetylase (R.norvegicus)		(-)				
RIKEN cD 4930579A11 gene	VMP1	(+)	(+)	RCC	C	
Mus musculus, clone MGC:29021 IMAGE:3495957, mR, complete cds	TAO1	(+)				
expressed sequence C81457	FLJ21022	(-)				
solute carrier family 25 (mitochondrial deoxynucleotide carrier), member 19	SLC25A19	(-)				

proctin S (alpha)	PROS1	(+)				
bone marrow stromal cell antigen 1	BST1	(+)				
centrin 2	CETN2	(-)				
RIKEN cD 3321401G04 gene	KIAA0738	(+)				
zuotin related factor 2	ZRF1	(+)				
split hand/foot deleted gene 1	DSS1	(+)	(+)	RCC	C	
solute carrier family 1, member 1	SLC1A1	(+)	(-)	RCC	DC	
RIKEN cD 1110001I24 gene	BZW2	(+)				
glutaryl-Coenzyme A dehydrogenase	GCDH	(-)				
RIKEN cD 4921528E07 gene	4921528E07Rik	(+)				
RIKEN cD 1810013B01 gene	1810013B01Rik	(-)				
expressed sequence AU042434	AU042434	(+)				
Mus musculus, Similar to CGI-147 protein, clone MGC:25743 IMAGE:3990061, mR, complete cds		(+)				
ubiquitin specific protease 7 (expressed sequence AA409944)	USP7	(+)				
N-acetylneuraminate pyruvate lyase	C1orf13	(+)				
L-3-hydroxyacyl-Coenzyme A dehydrogenase, short chain	HADHSC	(-)	(-)	RCC	C	
major vault protein	MVP	(+)				
growth arrest specific 2	GAS2	(-)	(-)	RCC	C	
RIKEN cD 1110002C08 gene	MGC9564	(-)				
acetyl-Coenzyme A transporter	ACATN	(-)				
RIKEN cD 5133400A03 gene	5133400A03Rik	(+)				
ALL1-fused gene from chromosome 1q	AF1Q	(-)				
myosin 1c	MYO1C	(+)				
ESTs		(-)				
NCK-associated protein 1	NCKAP1	(+)				
integrin alpha 6	ITGA6	(+)	(+)	RCC	C	
Mus musculus LDLR dan mR, complete cds		(-)				
RIKEN cD 1110032A13 gene	FLJ21172	(+)				
metastasis associated 1-like 1	MTA1L1	(+)				
fibulin 5	FBLN5	(-)				
expressed sequence C85317	C85317	(+)				
ESTs		(+)				
crystallin, lambda 1	CRYL1	(-)				
RIKEN cD 1700016A15 gene	FLJ11806	(+)				
5-azacytidine induced gene 1	Azi1	(-)				
estrogen related receptor, alpha	ESRRA	(-)				
spermatogenesis associated factor	SPATA5	(+)				

RIKEN cD 4930533K18 gene		(+)				
Harvey rat sarcoma oncogene, subgroup R	RRAS	(+)				
complement component 1, q subcomponent, beta polypeptide	C1QB	(+)	(+)	RCC	C	
S-adenosylhomocysteine hydrolase	AHCY	(-)	(-)	RCC	C	
brain protein 44-like	BRP44I	(-)	(-)	RCC	C	
inositol polyphosphate-5-phosphatase, 75 kDa	INPP5B	(-)				
hyaluronic acid binding protein 2	HABP2	(-)				
syndecan 1	SDC1	(+)	(-)	RCC	DC	
guanosine monophosphate reductase	GMPR	(+)				
alcohol dehydrogenase 4 (class II), pi polypeptide	ADH4	(-)	(-)	RCC	C	
branched chain ketoacid dehydrogenase E1, alpha polypeptide	BCKDHA	(-)	(+)	RCC	DC	
ESTs, Weakly similar to brain-specific angiogenesis inhibitor 1-associated protein 2 (Mus musculus) (M.musculus)		(-)				
Unknown		(-)				
R binding motif protein 3	RBM3	(+)				
superoxide dismutase 2, mitochondrial	SOD2	(-)	(+)	RCC	DC	(+)
histone deacetylase 1	HDAC1	(+)				(+)
biglycan	BGN	(+)				
ras homolog 9 (RhoC)	ARHC	(+)				
latexin	LXN	(+)	(+)	RCC	C	
pyruvate kinase 3	PKM2	(+)				(+)
SMC (structural maintenance of chromosomes 1)-like 1 (S. cerevisiae)	SMC1L1	(+)	(-)	RCC	DC	
serum/glucocorticoid regulated kinase 2	SGK2	(-)				
WD repeat domain 1	WDR1	(+)				
RIKEN cD 2310001A20 gene	C20orf3	(-)				
thymidine kinase 1	TK1	(+)	(+)	RCC	C	
glutathione S-transferase, alpha 4	GSTA4	(-)				
PH domain containing protein in retina 1	PHRET1	(-)				
RIKEN cD 1110020L19 gene	TREX2	(+)				
tumor necrosis factor receptor superfamily, member 1b	TNFRSF1B	(+)				
UDP-Gal:betaGlc beta 1,4-galactosyltransferase, polypeptide 2	B4GALT2	(+)				
N-myc downstream regulated 2	NDRG2	(-)				(+)
platelet derived growth factor, alpha	PDGFA	(+)				
hemochromatosis	HFE	(+)				

serine protease inhibitor, Kunitz type 2	SPINT2	(+)				
CD53 antigen	CD53	(+)	(+)	RCC	C	
leucine zipper-EF-hand containing transmembrane protein 1	LETM1	(-)				
Mus musculus, Similar to xylulokinase homolog (H. influenzae), clone IMAGE:5043428, mR, partial cds		(-)				
expressed sequence AW261723	SLC17A3	(-)				
phytanoyl-CoA hydroxylase	PHYH	(-)	(-)	RCC	C	
RIKEN cD 2610511O17 gene	FLJ20272	(+)				
RIKEN cD 2610306D21 gene	ANAPC4	(+)				
ESTs	FLJ22184	(-)				
adaptor-related protein complex AP-3, sigma 1 subunit	AP3S1	(+)	(+)	RCC	C	
Mus musculus, Similar to hypothetical protein MGC4368, clone MGC:28978 IMAGE:4503381, mR, complete cds	MGC4368	(-)				
phenylalkylamine Ca2+ antagonist (emopamil) binding protein	EBP	(-)				
MORF-related gene X	MORF4L2	(+)	(+)	RCC	C	
AU R binding protein/enoyl-coenzyme A hydratase	AUH	(-)				
SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily e, member 1	SMARCE1	(+)	(+)	RCC	C	
RIKEN cD 1810054O13 gene	1810054O13Rik	(-)				
spermidine/spermine N1-acetyl transferase	SAT	(+)				(+)
γ-rat simian leukemia viral oncogene homolog A (ras related)	RALA	(+)	(+)	RCC	C	
Mus musculus, clone MGC:37818 IMAGE:5098655, mR, complete cds	MGC37818	(-)				
expressed sequence AI117581	AI117581	(-)				
RIKEN cD 6230410I01 gene	FLJ10849	(+)				
RIKEN cD 2310075M15 gene	2310075M15Rik	(+)				
RIKEN cD 0610025I19 gene	0610025I19Rik	(-)				
expressed sequence AI118577	ZNF14	(-)				
neuropilin	NRP1	(+)	(+)	RCC	C	
G-rich RNA sequence binding factor 1 (D5Wsu31e) D segment, Chr 5, Wayne State University 31, expressed	GRSF1	(-)	(+)	RCC	DC	(+)



solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3	SLC13A3	(-)	(-)	RCC	C	
ubiquitin-like 1 (sentrin) activating enzyme E1B	UBA2	(+)				
RIKEN cD 1500041J02 gene	FLJ13448	(-)				
D segment, Chr 8, Brigham & Women's Genetics 1320 expressed	D8Bwg1320e	(-)				
expressed sequence C86302	C86302	(+)				
expressed sequence A1987692	A1987692	(+)				
parvalbumin	PVALB	(-)	(+)(-)	RCC	conflict	
small nuclear ribonucleoprotein E	SNRPE	(+)	(+)	RCC	C	
RIKEN cD 6530411B15 gene	DKFZp564K1964.1	(-)				
MARCKS-like protein	MLP	(+)				
ras homolog D (RhoD)	ARHD	(+)				
Mus musculus, clone IMAGE:3967158, mR, partial cds	C13orf11	(-)				
RIKEN cD 1700037H04 gene	FLJ20550	(+)				
deiodise, iodothyronine, type I	DIO1	(-)				
RIKEN cD 0610011C19 gene	FLJ22386	(-)				
v-ral simian leukemia viral oncogene homolog B (ras related)	RALB	(+)				
ESTs, Weakly similar to MAJOR URINARY PROTEIN 4 PRECURSOR (M.musculus)		(-)				
protein C	PROC	(-)	(-)	RCC	C	
alpha-methylacyl-CoA racemase	AMACR	(-)	(+)	RCC	DC	
RIKEN cD 2810411G23 gene	TPD52L2	(+)	(+)	RCC	C	
Unknown		(-)				
DJ (Hsp40) homolog, subfamily A, member 1	DNAJA1	(-)				
RIKEN cD 1200003E16 gene	1200003E16Rik	(-)				
heterogeneous nuclear ribonucleoprotein A1	HNRPA1	(+)	(+)	RCC	C	
FK506 binding protein 1a (12 kDa)	FKBP1A	(+)				(+)
RIKEN cD 4933405K01 gene	MGC14799	(+)				
surfeit gene 4	SURF4	(+)	(+)	RCC	C	
mitogen activated protein kinase 13	MAPK13	(+)				
RIKEN cD 2310022K15 gene	KI.HDC2	(+)				
RIKEN cD 1300002P22 gene	ECH1	(-)				
ectonucleotide pyrophosphatase/phosphodiesterase 2	ENPP2	(-)	(+)	RCC	DC	
PCTAIRE-motif protein kinase 3	PCTK3	(-)	(+)	RCC	DC	
splicing factor 3b, subunit 1, 155 kDa	SF3B1	(+)	(+)	RCC	C	
zinc finger protein 36, C3H type-like 2	ZFP36L2	(+)				

M.musculus mR for protein expressed at high levels in testis	Tex2	(-)				
nuclear receptor coactivator 4	NCOA4	(-)	(+)	RCC	DC	
PC4 and SFRS1 interacting protein 2 (expressed sequence AU015605)	PSIP2	(+)				
purinergic receptor (family A group 5); RIKEN cD 26103:02102 gene	P2RY5	(+)				
ESTs, Moderately similar to SEC7 homolog (Homo sapiens) (H.sapiens)		(-)				
Mus musculus, clone IMAGE:4456744, mR, partial cds	G630055P03Ri	(+)				
Blu protein	ZMYND10	(-)				
solute carrier family 6 (neurotransmitter transporter, glycine), member 9 / glycine transporter 1	SLC6A9	(+)				
Mus musculus, Similar to MIPP65 protein, clone MGC:18783 IMAGE:4188234, mR, complete cds	1500032D16Rik	(-)				
expressed sequence AU018056	AU018056	(-)				
RIKEN cD 1810009M01 gene	LR8	(+)				
serum/glucocorticoid regulated kise	SGK	(-)				
Mus musculus, Similar to unc93 (C.elegans) homolog B, clone MGC:25627 IMAGE:4209296, mR, complete cds	UNC93B1	(+)				
RIKEN cD 2810473M14 gene	2810473M14Rik	(-)				
TATA box binding protein-like protein	TBPL1	(+)				
acyl-Coenzyme A dehydrogenase, short/branched chain	ACADSB	(-)	(-)	RCC	C	
Mus musculus, clone MGC:12159 IMAGE:37111169, mR, complete cds	D530037I19Rik	(+)				
proline dehydrogenase	PRODH	(-)				(+)
leukemia-associated gene	STMN1	(+)	(+)	RCC	C	
Mus musculus evectin-2 (Bvt2) mR, complete cds	PLEKHB2	(-)				
kise insert domain protein receptor	KDR	(-)	(+)	RCC	DC	
RIKEN cD 1300019I21 gene	MTAP	(+)				
slit homolog 3 (Drosophila)	SLIT3	(+)				
RIKEN cD 6330565B14 gene	ADH8	(-)				
RIKEN cD 1810043O07 gene	KIAA0601	(+)				
RIKEN cD 1110008B24 gene	C14orf11	(+)				

thyroid hormone responsive SPOT14 homolog (Rattus)	THRSP	(-)				
RIKEN cD 2310079C17 gene	DKFZP547E2110	(+)				
integral membrane protein 1	ITM1	(+)				
expressed sequence R75232	R75232	(+)				
coronin, actin binding protein 1B	CORO1B	(+)	(-)	RCC	DC	
RIKEN cD 2310004I03 gene	2310004I03Rik	(-)				
RIKEN cD 1010001M04 gene	1010001M04Rik	(-)				
RIKEN cD 2700038M07 gene - pending	WSB1	(+)	(-)	RCC	DC	
RIKEN cD 1100001J13 gene - pending	KIAA1049	(-)	(+)	RCC	DC	
RIKEN cD 0610016J10 gene	CGI-27	(+)				
SET translocation	SET	(+)	(+)	RCC	C	(+)
ESTs, Highly similar to prefoldin 4 (Homo sapiens) (H.sapiens)	PFDN4	(+)	(+)	RCC	C	
Mus musculus, Similar to nucleolar cysteine-rich protein, clone MGC:6718 IMAGE:3586161, mR, complete cds --pending	HSA6591	(+)	(+)	RCC	C	
Mus musculus, Similar to sirutin silent mating type information regulation 2 homolog 7 (S. cerevisiae), clone MGC:37560 IMAGE:4987746, mR, complete cds	SIRT7	(-)				
Mus musculus, clone MGC:36554 IMAGE:4954874, mR, complete cds	D14Ert226e	(+)				
RIKEN cD 2610206D03 gene	2610206D03Rik	(+)				
peroxisomal delta3, delta2-enoyl-Coenzyme A isomerase	PECI	(-)	(-)	RCC	C	
(Sdcagg28) serologically defined colon cancer antigen 28	STARD10	(-)				
protein tyrosine phosphatase 4a1	PTP4A1	(+)				
peroxisomal biogenesis factor 13	PEX13	(-)				
ESTs		(-)				
expressed sequence AI957255	KIAA0564	(-)				
cleavage and polyadenylation specific factor 5, 25 kD subunit	CPSF5	(+)				
intercellular adhesion molecule	ICAM1	(+)	(+)	RCC	C	(+)
RIKEN cD 1200013A08 gene	MGC3047	(+)				
D primase, p49 subunit	PRIM1	(+)				
RIKEN cD 2410029D23 gene	ATP6V1E1	(-)				
RIKEN cD 1300017C12 gene	FLJ10948	(-)	(-)	RCC	C	

steroid receptor R activator 1	SRA1	(+)				
regulator for ribosome resistance homolog (S. cerevisiae)	RRS1	(+)				
RIKEN cD 0610006N12 gene	NDUFB4	(-)				
poly(rC) binding protein 1	PCBP1	(+)	(+)	RCC	C	
expressed sequence AU015645	AU015645	(-)				
ESTs		(+)				
Mus musculus mR for alpha-albumin protein	AFM	(-)	(-)	RCC	C	
small nuclear ribonucleoprotein D2	SNRPD2	(+)	(+)	RCC	C	
succinate dehydrogenase complex, subunit B, iron sulfur (lp); RIKEN cD 0710008N11 gene	SDHB	(-)	(-)	RCC	C	
homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	HERPUD1	(-)				
solute carrier family 16 (monocarboxylic acid transporters), member 7	SLC16A7	(-)	(+)	RCC	DC	
activity-dependent neuroprotective protein	ADNP	(+)				
RIKEN cD 1810027P18 gene	DCXR	(-)	(-)	RCC	C	
insulin-like growth factor binding protein 3	IGFBP3	(-)	(+)	RCC	DC	(+)
smoothed homolog (Drosophila)	SMOH	(-)				
SEC13 related gene (S. cerevisiae) RIKEN cD 1110003H02 gene	SEC13L1	(+)				
Mus musculus, Similar to chromosome 20 open reading frame 36, clone IMAGE:5356821, mR, partial cds	FLJ10883	(-)				
flotillin 1	FLOT1	(+)				
RIKEN cD 2700055K07 gene	CGI-38	(+)				
matrix metalloproteinase 23	MMP23A	(+)				
Mus musculus, Similar to KIAA1075 protein, clone IMAGE:5099327, mR, partial cds	TENC1	(-)				
RIKEN cD 1110007F23 gene	1110007F23Rik	(+)				
glycine N-methyltransferase	GNMT	(-)				
zinc finger like protein 1	ZFPL1	(-)				
capping protein beta 1	CAPZB	(+)				
RIKEN cD 6720463E02 gene		(+)				
expressed sequence AA408783	SPEC2	(+)	(+)	RCC	C	
elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 1	ELOVL1	(+)				

carnitine palmitoyltransferase 2	CPT2	(-)	(-)	RCC	C	
Mus musculus, Similar to hypothetical protein FLJ20335, clone MGC:28912 IMAGE:4922274, mRNA, complete cds	D14Erd813e	(+)				
flap structure specific endonuclease 1	FEN1	(+)	(+)	RCC	C	
chloride intracellular channel 1	CLIC1	(+)	(+)	RCC	C	
ATPase, H <sup>+</sup> transporting, V1 subunit F; RIKEN cD 1110004G16 gene	ATP6V1F	(-)				
BRG1/brm-associated factor 53A	BAF53A	(+)				
matrix metalloproteinase 2	MMP2	(+)	(-)	RCC	DC	(+)
methylene tetrahydrofolate dehydrogenase (DP+ dependent), methylenetetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthase	MTHFD1	(-)	(+)	RCC	DC	
damage specific D binding protein 1 (127 kDa)	DDB1	(+)				
glutathione transferase zeta 1 (maleylacetoacetate isomerase)	GSTZ1	(-)				
isocitrate dehydrogenase 2 (DP+), mitochondrial	IDH2	(-)				
ubiquitin-like 1 (sentrin) activating enzyme E1A	SAE1	(+)	(+)	RCC	C	
actin, beta, cytoplasmic	ACTB	(+)	(+)	RCC	C	
lectin, galactose binding, soluble 3	LGALS3	(+)	(+)	RCC	C	
upregulated during skeletal muscle growth 5	MGC14697	(-)				
polycystic kidney disease 1 homolog	PKD1	(-)	(+)	RCC	DC	(+)
Mus musculus, Similar to hypothetical protein MGC3133, clone MGC:11596 IMAGE:3965951, mRNA, complete cds	SF3b10	(+)				
RIKEN cD 1700015P13 gene	1700015P13Rik	(-)				
MYC-associated zinc finger protein (purine-binding transcription factor)	MAZ	(+)	(+)	RCC	C	
proteasome (prosome, macropain) 26S subunit, non-ATPase, 13	PSMD13	(+)	(+)	RCC	C	
pyruvate dehydrogenase 2	PDK2	(-)				
ATPase, H <sup>+</sup> transporting, lysosomal (vacuolar proton pump), alpha 70 kDa, isoform 1	ATP6V1A1	(-)				(+)
N-acetylglucosaminase	NAGK	(+)	(+)	RCC	C	
arginine-rich, mutated in early stage tumors	ARMET	(+)				

sigling intermediate in Toll pathway- evolutionarily conserved	Sitpoc	(-)	(-)	RCC	C	
cell division cycle 25 homolog A (S. cerevisiae)	CDC25A	(+)				
B-box and SPRY domain containing	BSPRY	(+)				
Mus musculus, clone MGC:6545 IMAGE:2655444, mR, complete cds	MAT2A	(-)	(+)	RCC	DC	
expressed sequence C86169	C86169	(-)				
immunoglobulin superfamily, member 8	IGSF8	(+)				
RIKEN cD 2410002J21 gene	ENIGMA	(+)				(+)
myeloid-associated differentiation marker	MYADM	(+)				
RIKEN cD 503141206 gene	Dutp	(+)				
RIKEN cD 2310032J20 gene	BDH	(-)				
serine hydroxymethyl transferase 2 (mitochondrial); RIKEN cD 2700043D08 gene	SHMT2	(-)	(+)	RCC	DC	
ribosomal protein L21	RPL21	(+)	(+)	RCC	C	(+)
thioether S-methyltransferase	Temt	(-)				
interferon inducible protein 1	Ifi1	(-)				
Hprt	HPRT1	(+)				
retinoblastoma-like 1 (p107)	RBL1	(+)				
RAB3D, member RAS oncogene family	RAB3D	(+)				
glycine amidinotransferase (L- arginine:glycine amidinotransferase)	GATM	(-)	(-)	RCC	C	
ribosomal protein S23	RPS23	(+)	(+)	RCC	C	
expressed sequence C87222	C87222	(+)				
RIKEN cD 1300013F15 gene	FLJ22390	(-)				
erythrocyte protein band 4.1 / Mus musculus adult male tongue cD, RIKEN full-length enriched library, clone:7310065B16:erythrocyte protein band 4.1, full insert sequence	EPB41	(-)	(-)	RCC	C	
RIKEN cD 5730406I15 gene	KIAA0102	(+)				
mitochondrial ribosomal protein L50; (D4Wsu125e) D segment, Chr 4, Wayne State University 125, expressed	MRPL50	(-)				
myristoylated alanine rich protein kise C substrate	MACS	(+)				
ribosomal protein L8	RPL8	(+)	(+)	RCC	C	
lysosomal-associated protein transmembrane 4A	LAPTM4A	(+)				
Mus musculus, clone MGC:19042 IMAGE:4188988, mR, complete cds	OGDH	(-)				

RIKEN cD 1810058K22 gene	CDC42EP1	(+)				
Mus musculus, Similar to dendritic cell protein, clone MGC:11741 IMAGE:3969335, mR, complete cds	GA17	(+)				
eukaryotic translation initiation factor 3, subunit 4 (delta, 44 kDa)	EIF3S4	(+)	(+)	RCC	C	
RIKEN cD 2510015F01 gene	FLJ12442	(+)				
nuclear protein 15.6	P17.3	(-)				
glucose-6-phosphatase, transport protein 1	G6PT1	(-)				
solute carrier family 22 (organic anion transporter), member 6	SLC22A6	(-)	(-)	RCC	C	
expressed sequence AI132189	AI132189	(-)				
coagulation factor XIII, beta subunit	F13B	(-)				
TEA domain family member 2	TEAD2	(+)				
casein kinase 1, epsilon	CSNK1E	(+)				
ESTs		(-)				
proteasome (prosome, macropain) subunit, alpha type 6	PSMA6	(+)	(+)	RCC	C	
syntrophin, basic 2	SNTB2	(+)				
ubiquitin-conjugating enzyme E2N	UBE2N	(+)				
Mus musculus, clone IMAGE:3589087, mR, partial cds		(-)				
D segment, Chr 18, Wayne State University 181, expressed	ALDH7A1	(-)	(-)	RCC	C	
Kruppel-like factor 5	KLF5	(+)	(+)	RCC	C	
X transporter protein 2	Xtp2	(-)				
CDC28 protein kinase 1	CKS1B	(+)	(+)	RCC	C	
expressed sequence AI461788	AI461788	(-)				
phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 1 (p85 alpha)	PIK3R1	(+)				
sex-lethal interactor homolog (Drosophila)	RPC5	(-)				
expressed sequence AW124722	AW124722	(-)				
ubiquitin-conjugating enzyme E2L3	UBE2L3	(+)				
expressed sequence AI836219	AI836219	(-)				
ESTs, Weekly similar to TS13 MOUSE TESTIS-SPECIFIC PROTEIN PBS13 (M.musculus)	MGC39016	(+)				
expressed sequence AI480660	AI480660	(-)				
ribosomal protein L19	RPL19	(+)	(+)	RCC	C	
Mus musculus, clone MGC:12039 IMAGE:3603661, mR, complete cds	Itp5	(-)				
inhibin beta-B	INHBB	(+)	(+)	RCC	C	

serine (or cysteine) protease inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	SERPINE2	(+)				
ESTs		(+)				
dihydropyrimidase	DPYS	(-)	(-)	RCC	C	
glutathione S-transferase, mu 6	GSTM1	(+)				
PYRIN-containing APAF1-like protein 5 / expressed sequence AI504961	PYPAF5	(-)				
RIKEN cD 1200011D11 gene	BK65A6.2	(-)				
kinectin 1	KTN1	(+)				
ribosomal protein L28	RPL28	(+)	(+)	RCC	C	
ESTs		(+)				
four and a half LIM domains 1	FHL1	(-)	(+)	RCC	DC	(+)
phosphatidylinositol transfer protein	PTPN	(+)				
growth differentiation factor 15	PLAB	(+)	(+)	RCC	C	(+)
ESTs		(-)				
expressed sequence AI646725	MDS028	(-)				
insulin-like growth factor binding protein, acid labile subunit	IGFALS	(-)				
carboxypeptidase E	CPE	(+)				
peptidylprolyl isomerase C-associated protein	LGALS3BP	(+)	(+)	RCC	C	
vascular endothelial growth factor A	VEGF	(-)	(+)	RCC	DC	(+)
expressed sequence AI465301	AI465301	(-)				
malate dehydrogenase, soluble	MDH1	(-)				
potassium channel, subfamily K, member 2	KCNK2	(-)				
ribosomal protein, large, P1	RPLP1	(+)	(+)	RCC	C	
expressed sequence AI448003	AI448003	(+)				
expressed sequence AI504062	AI504062	(+)				
poly (A) polymerase alpha	PAPOLA	(-)	(+)	RCC	DC	
DPH oxidase 4	NOX4	(-)	(?)	RCC	conflict	
small inducible cytokine subfamily D, 1	SCYD1	(+)				
secreted phosphoprotein 1	SPP1	(+)	(-)/(+)	RCC	conflict	
ESTs		(-)				
ESTs		(-)				
AMP deamase 3	AMPD3	(+)				
glycerol kase	GK	(-)	(-)	RCC	C	
J domain protein 1	JDP1	(-)				
Mus musculus, clone IMAGE:3155544, mRNA, partial cds	LOC224650	(-)				
RIKEN cD 1110038L14 gene	CKS2	(+)	(+)	RCC	C	
cornichon homolog (Drosophila)	CNIH	(+)				
ubiquitin-conjugating enzyme E21	UBE21	(+)				(+)
Bcl-2-related ovarian killer protein	BOK	(+)				



tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide	YWHAH	(+)	(+)	RCC	C	
(Gus-s) beta-glucuronidase structural	GUSB	(+)				
RIKEN cD A930008K15 gene	KIAA0605	(-)				
myosin light chain, alkali, nonmuscle	MYL6	(+)	(-)	RCC	DC	
apolipoprotein B editing complex 1	APOBEC1	(+)				
soc-2 (suppressor of clear) homolog (C. elegans)	SHOC2	(+)				
RIKEN cD 1200016G03 gene	1200016G03Rik	(-)				
ESTs	9130203F04Rik	(+)				
hydroxysteroid dehydrogenase-3, delta<math>\delta</math>-3-beta	Hsd3b3	(-)				
expressed sequence AI507121	AI507121	(-)				
claudin 1	CLDN1	(+)	(+)	RCC	C	
serine protease inhibitor 6	SERPINF9	(+)				
small inducible cytokine A5	SCYA5	(+)	(+)	RCC	C	
serine hydroxymethyl transferase 1 (soluble)	SHMT1	(-)	(+)	RCC	DC	
RIKEN cD 3021401A05 gene	3021401A05Rik	(+)				
ESTs		(-)				
Tnf receptor-associated factor 2	TRAF2	(+)				
talin 2	TLN2	(-)				
high mobility group box 3	HMGB3	(+)	(+)	RCC	C	
RIKEN cD 1700012B18 gene	OKL38	(-)				
ornithine decarboxylase, structural	ODC1	(+)				
gap junction membrane channel protein beta 2	GJB2	(-)	(+)	RCC	DC	
solute carrier family 2 (facilitated glucose transporter), member 5	SLC2A5	(-)	(-)	RCC	C	
ESTs, Moderately similar to T08673 hypothetical protein DKFZp564C0222.1 (H.sapiens)	KIAA0977	(-)	(-)	RCC	C	
nuclear factor of kappa light chain gene enhancer in B-cells 1, p105	NFKB1	(+)				
Williams-Beuren syndrome chromosome region 14 homolog (human)	WBSCR14	(-)	(-)	RCC	C	
RIKEN cD 1300018I05 gene	KIAA0082	(+)				
RIKEN cD 1110005N04 gene	TAF5L	(+)				
caspase 3, apoptosis related cysteine protease	CASP3	(+)				(-)
glycoprotein 49 B	Gp49b	(+)				

histocompatibility 2, Q region locus 7	H2-Q7	(+)				
ESTs		(+)				
cyclin-dependent kinase inhibitor 1A (P21)	CDKN1A	(+)	(+)/(+?)	RCC	conflict	(+)
Rho guanine nucleotide exchange factor (GEF) 3	ARHGEF3	(-)				
complement component 1, q subcomponent, c polypeptide	C1QG	(+)				
RIKEN cD 9530058B02 gene	MGC15416	(-)				
D segment, Chr 17, ERATO Doi 441, expressed	D17Ert441e	(+)				
expressed sequence A1844685	MGC15429	(-)				
slit homolog 2 (Drosophila)	SLIT2	(-)				
tetranectin (plasminogen binding protein)	T	(-)				
citrate lyase beta like	CLYBL	(-)				
succinate-Coenzyme A ligase, GDP-forming, beta subunit	SUCLG2	(-)				(+)
cytokine inducible SH2-containing protein 3	SOC3	(+)				
solute carrier family 4 (anion exchanger), member 4	SLC4A4	(-)	(-)	RCC	C	
heat shock protein, 105 kDa	HSPH1	(-)	(+)	RCC	DC	
RIKEN cD 4733401N12 gene	CPSF6	(+)				
ESTs		(-)				
ribosomal protein L3	RPL3	(+)				(+)
carbamate palmitoyltransferase 1, muscle	CPT1B	(-)				
ESTs		(+)				
RIKEN cD 2310010G13 gene	2310010G13Rik	(-)				
ESTs		(-)				
expressed sequence A1558103	LRRN1	(-)				
Unknown		(-)				
RIKEN cD 4932442K08 gene	4932442K08Rik	(+)				
argase type II	ARG2	(+)				
RIKEN cD D630002J15 gene	D630002J15Rik	(-)				
ESTs		(+)				
papillary renal cell carcinoma (translocation-associated)	PRCC	(+)	(?)	RCC	conflict	
growth differentiation factor 8	GDF8	(+)				
thioredoxin 2	TXN2	(-)				
renin 2 tandem duplication of Ren1	Ren2	(-)				
Unknown		(+)				
calbindin-28K	CALB1	(-)	(-)	RCC	C	
secreted acidic cysteine rich glycoprotein	SPARC	(+)	(+)	RCC	C	

calcium channel, voltage-dependent, beta 3 subunit	CACNB3	(+)	(+)	RCC	C	
expressed sequence AI604920	KIAA0297 KIAA0329	(+)				
RIKEN cD 5133401H06 gene	5133401H06Rik	(-)				
expressed sequence AI314027	GLS	(+)				
PPAR gamma coactivator-1beta protein	PERC	(-)				
chaperonin subunit 3 (gamma)	CCT3	(+)				
coproporphyrinogen oxidase	CPO	(-)				
erythroid differentiation regulator	edr	(+)				
polymerase, gamma	POLG	(-)				
cathepsin S	CTSS	(+)	(+)	RCC	C	
expressed sequence AI844876	AI844876	(-)				
RIKEN cD 3010001A07 gene	BFAR	(-)				
expressed sequence AI586180	AI586180	(+)				
tetratricopeptide repeat domain	TTC3	(+)	(+)	RCC	C	
Mus musculus, clone MGC:6377 IMAGE:3499365, mR, complete cds	ME2	(+)				
smoothelin	SMTN	(+)				
complement component 1, q subcomponent, alpha polypeptide	CIQA	(+)	(+)	RCC	C	
Unknown		(-)				
glycerol phosphate dehydrogenase 1, mitochondrial	GPD2	(-)				
ribosomal protein S26	RPS26	(+)				
protein tyrosine phosphatase, receptor type, B	PTPRB	(-)	(+)	RCC	DC	
expressed sequence AW493404	AW493404	(+)				
RIKEN cD 4930506M07 gene	FLJ11122	(+)				
solute carrier family 35, member A5; RIKEN cD 1010001J06 gene	SLC35A5	(-)				
Mus musculus, clone MGC:36388 IMAGE:5098924, mR, complete cds	MCSC	(-)				
coagulation factor III	F3	(+)				
ESTs, Weakly similar to ADT1 MOUSE ADP,ATP CARRIER PROTEIN, HEART/SKELETAL MUSCLE ISOFORM T1 (M.musculus)	SLC25A16	(-)				
expressed sequence AI449309	AI449309	(+)				
max binding protein	MNT	(+)				
fatty acid synthase	FASN	(-)				(+)
hypothetical protein, MGC:6957	MGC6957	(+)				

(2610524K04Rik ; RIKEN cD 2610524K04 gene)	pp90RSK4	(+)				
expressed sequence A W045860	AW045860	(-)				
ESTs		(-)				
ribosomal protein L7	RPL7	(+)	(+)	RCC	C	
solute carrier family 34 (sodium phosphate), member 2	SLC34A2	(+)				
fumarylacetoacetate hydrolase	FAH	(-)	(-)	RCC	C	
Mus musculus, Similar to ribosomal protein S20, clone MGC:6876 IMAGE:2651405, mR, complete cds		(+)				
single Ig IL-1 receptor related protein	SIGIRR	(-)	(-)	RCC	C	
expressed sequence AI528491	AI528491	(-)				
RIKEN cD 2810468K17 gene	MGC13272	(+)				
ESTs		(-)				
mitogen-activated protein kinase 7	MAPK7	(+)				(+)
Mus musculus, clone MGC:19361 IMAGE:4242170, mR, complete cds		(+)				
schlafen 4	FLJ10260	(+)				
RIKEN cD 1810036E22 gene		(-)				
flotillin 2	FLOT2	(+)				
nicotinamide nucleotide transhydrogenase	NNT	(-)	(-)	RCC	C	
expressed sequence AI661919	AI661919	(-)				
deoxyribonuclease I	DNASE1	(-)				
Mus musculus, Similar to ubiquitin-conjugating enzyme E2 variant 1, clone MGC:7660 IMAGE:3496088, mR, complete cds	UBE2V1	(-)	(+)	RCC	DC	
Mus musculus, clone IMAGE:3586777, mR, partial cds	DLAT	(-)				
RIKEN cD 1200015A22 gene	MGC3222	(+)				
RIKEN cD 5830445O15 gene	5830445O15Rik	(-)				
2-hydroxyphytanoyl-CoA lyase	HPCL2	(-)	(-)	RCC	C	
serine (or cysteine) protease inhibitor, clade G (C1 inhibitor), member 1	SERPING1	(+)	(+)	RCC	C	
FK506 binding protein 10 (65 kDa)	FKBP10	(+)				
calysentenin 1	CLSTN1	(-)	(-)	RCC	C	
RIKEN cD 2600001N01 gene	ZWINT	(+)				
adenylosuccinate synthetase 2, non muscle	ADSS	(+)				
cryptochrome 2 (photolyase-like)	CRY2	(-)				

solute carrier family 12, member 1	SLC12A1	(-)	(-)	RCC	C	(+)
S100 calcium binding protein A4	S100A4	(+)				
E74-like factor 3	ELF3	(+)	(+)	RCC	C	
RIKEN cD 2900074L19 gene		(-)				
laminin, alpha 2	LAMA2	(+)	(+)	RCC	C	
solute carrier family 25 (mitochondrial carrier)	SLC25A10	(-)				
Mus musculus, clone MGC:18871 IMAGE:4234793, mR, complete cds	GLYAT	(-)	(-)	RCC	C	
macrophage expressed gene 1	MPEG1	(+)				
RIKEN cD 2810430J06 gene	FRCP1	(+)				
expressed sequence AW552393	AW552393	(-)				
cofilin 1, non-muscle	CFL1	(+)	(+)(-)	RCC	conflict	
expressed sequence AI875199	AI875199	(-)				
expressed sequence BB120430	BB120430	(+)				
ESTs, Weakly similar to B Chain B, Crystal Structure Of Murine Soluble Epoxide Hydrolase Complexed With Cdu Inhibitor (M.musculus)		(+)				
ESTs, Weakly similar to DRR1 (H.sapiens)		(-)				
Mus musculus, Similar to KIAA0763 gene product, clone IMAGE:4503056, mR, partial cds	KIAA0763	(-)				
expressed sequence AI875557	AI875557	(-)				
expressed sequence AI848669	AI848669	(-)				
RIKEN cD 2610305D13 gene	FLJ11191	(+)				
liver-specific bHLH-Zip transcription factor	Lisch7	(+)				(+)
phosphodiesterase 1A, calmodulin-dependent	PDE1A	(-)	(-)	RCC	C	
ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit, isoform 1	ATP5A1	(-)				
laminin receptor 1 (67kD, ribosomal protein SA)	LAMR1	(+)	(+)	RCC	C	
ESTs		(-)				
runt related transcription factor 1	RUNX1	(+)				
leukotriene C4 synthase	LTC4S	(+)				
RIKEN cD 9130022E05 gene	9130022E05Rik	(-)				
methyl CpG binding protein 2	MECP2	(-)				
expressed sequence AI835705	AI835705	(-)				
a disintegrin and metalloprotease domain 12 (metrin alpha)	ADAM12	(+)				
Mus musculus chemokine receptor CCX CKR mR, complete cds, alternatively spliced	CCRL1	(-)				
AXL receptor tyrosine kinase	AXL	(+)				

aldo-keto reductase family 1, member C18 ; expressed sequence AW146047	Akr1c18	(-)				
protein tyrosine phosphatase, receptor type, C polypeptide-associated protein	PTPRCAP	(+)				
kinesin family member 21A	KIF21A	(-)	(+)	RCC	DC	
Kruppel-like factor 15	KLF15	(-)				
RIKEN cD 2610039E05 gene	2610039E05Rik	(-)				
platelet derived growth factor receptor, beta polypeptide	PDGFRB	(+)				
expressed sequence AJ413466	PPP1R1B	(-)				
thrombospondin 1	THBS1	(+)	(-)	RCC	DC	
TRAF-interacting protein	TRIP	(+)				
RIKEN cD 2700099C19 gene	LOC51248	(+)				
SH3 domain protein 3	OSTF1	(+)				
5',3' nucleotidase, cytosolic	NTSC	(+)				
RIKEN cD 1700028A24 gene	LOC55862	(-)				
expressed sequence AW743884	AW743884	(+)				
epidermal growth factor-containing fibulin-like extracellular matrix protein 2	EFEMP2	(+)				
Mus musculus adult male liver cD, RIKEN full-length enriched library, clone: 1300015E02:deoxyribonuclease II alpha, full insert sequence	CSAD	(-)				
RIKEN cD 2010315L10 gene	MDS032	(+)				
ribosomal protein L18	RPL18	(+)	(+)	RCC	C	
microfibrillar associated protein 5	MGP2	(+)				
aldehyde dehydrogenase family 1, subfamily A2	ALDH1A2	(+)				
adenylate kinase 4	Ak4	(-)				
E74-like factor 4 (ets domain transcription factor)	ELF4	(+)				
G protein-coupled receptor kinase 7	MKNK2	(-)	(+)	RCC	DC	
forkhead box M1	FOXM1	(+)				
solute carrier family 22 (organic cation transporter), member 4	SLC22A4	(-)				
claudin 7	CLDN7	(+)				
proteasome (prosome, macropain) subunit, beta type 1	PSMB1	(+)				
solute carrier family 22 (organic cation transporter), member 5	SLC22A5	(-)				
UDP-glucuronosyltransferase 1 family, member 1	UGT1A@	(-)				
glutathione S-transferase, pi 2	Gstp2	(+)				
ESTs		(-)				
cystatin C	CST3	(+)				

transcription factor 4	TCF4	(+)				
RIKEN cD 2610301D06 gene	2610301D06Rik	(+)				
tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide	YWHAE	(+)				
methylmalonyl-Coenzyme A mutase	MUT	(-)				(+)
myosin light chain, alkali, cardiac atria	MYL4	(+)				
enhancer of zeste homolog 2 (Drosophila)	EZH2	(+)				
RIKEN cD 0610025G13 gene	RPL38	(+)	(-)/(+)	RCC	conflict	
Unknown	COL18A1	(+)				
Tial1 cytotoxic granule-associated R binding protein-like 1	TIAL1	(+)	(+)	RCC	C	
ribosomal protein S14	RPS14	(+)	(+)	RCC	C	
numb gene homolog (Drosophila)	NUMB	(+)				
RIKEN cD 1300004O04 gene	CACH-1	(-)				
adducin 3 (gamma)	ADD3	(-)	(+)	RCC	DC	(+)
vitamin D receptor	VDR	(-)				
ribosomal protein L5	RPL5	(+)				
RIKEN cD 1810023B24 gene	FLJ14503	(+)				
RIKEN cD 3010027G13 gene	DKFZp434C119.1	(-)				
high mobility group AT-hook 1	HMGAI	(+)				
endonuclease G	ENDOG	(-)				
septin 8	KIAA0202	(+)				
double cortin and calcium/calmodulin-dependent protein kinase-like 1	DCAMKL1	(+)				
procollagen, type I, alpha 2	COL1A2	(+)	(+)	RCC	C	
Mus musculus, hypothetical protein MGC11287 similar to ribosomal protein S6 kinase, clone MGC28043 IMAGE3672127, mRNA, complete cds	RPS6KL1	(-)				
kallikrein 6	Klk1	(-)	(+)	RCC	DC	
mini chromosomal maintenance deficient (S. cerevisiae)	MCM3	(+)	(+)	RCC	C	
cartilage oligomeric matrix protein	COMP	(-)				
panthophysin	HILF	(-)				
macrophage scavenger receptor 2	Msr2	(+)				
ESTs, Weakly similar to S65210 hypothetical protein YPL191c - yeast (Saccharomyces cerevisiae) (S. cerevisiae)		(-)				
expressed sequence AI593249	AI593249	(-)				
tumor rejection antigen gp96	TRA1	(+)	(+)	RCC	C	(+)
Unknown		(+)				

lysosome	LYZ	(+)	(+)	RCC	C	
ATPase, +/K+ transporting, beta 1 polypeptide	ATP1B1	(-)	(+)	RCC	DC	(+)
lysosomal-associated protein transmembrane 5	LAPTM5	(+)	(+)	RCC	C	
Yamaguchi sarcoma viral (v-yes) oncogene homolog	YES1	(+)				
gamma-glutamyl transpeptidase	GGT1	(-)				
chitinase 3-like 3	CHIA	(+)				
ESTs, Weakly similar to JE0096 myocilin - mouse (M.musculus)		(+)				
peptidylprolyl isomerase C	PPIC	(-)				
solute carrier family 7 (cationic amino acid transporter, y+ system), member 9	SLC7A9	(-)				
fibrillarin	FBL	(+)	(+)	RCC	C	
RIKEN cD 2610029K21 gene	FLJ20249	(+)				
mutS homolog 2 (E. coli)	MSH2	(+)	(+)	RCC	C	
TYRO protein tyrosine kinase binding protein	TYROBP	(+)	(+)	RCC	C	
RIKEN cD 6430559E15 gene	HT036	(-)				
ESTs	1110069O07Rik	(-)				
ras homolog gene family, member E	ARHE	(-)	(+)	RCC	DC	
stromal cell derived factor 1	CXCL12	(-)				
cadherin 3	CDH3	(+)				
small inducible cytokine B subfamily, member 5	SCYB6	(+)				
heparin binding epidermal growth factor-like growth factor	DTR	(+)				
AIE binding protein 1	AEBP1	(+)				
poliovirus receptor-related 3	PVRL3	(+)	(+)	RCC	C	
ESTs		(+)				
phospholipase A2, group IIA (platelets, synovial fluid)	PLA2G2A	(-)				
guanine nucleotide binding protein (G protein), gamma 2 subunit	GNG2	(+)				
nidogen 1	NID	(+)	(+)	RCC	C	
integrin beta 1 (fibronectin receptor beta)	ITGB1	(+)	(+)	RCC	C	
protein tyrosine phosphatase, receptor type, O	PTPRO	(+)	(-)	RCC	DC	
retinoic acid induced 1	RAI1	(+)				
cell division cycle 2 homolog A (S. pombe)	CDC2	(+)				
homeo box B7	HOXB7	(+)				
matrix metalloproteinase 7	MMP7	(+)	(+)	RCC	C	
Kruppel-like factor 1 (erythroid)	KLF1	(-)				
ESTs		(-)				
feline sarcoma oncogene	FES	(+)	(+)	RCC	C	
reticulocalbin	RCN1	(+)	(+)	RCC	C	
aconitase 1	ACO1	(-)	(-)	RCC	C	



CCCTC-binding factor	CTCF	(+)				
integrin alpha M	ITGAM	(+)	(+)	RCC	C	
serine (or cysteine) protease inhibitor, clade B (ovalbumin), member 2	SERPINF2	(+)				
solute carrier family 16 (monocarboxylic acid transporters), member 2	SLC16A2	(-)	(-)	RCC	C	
Hoxc8	MCM5	(+)				
Mus musculus, Similar to angiopoietin-like factor, clone MGC:32448 IMAGE:5043159, mR, complete cds		(-)				
ESTs		(-)				
ring finger protein (C3HC4 type) 19	RNF19	(+)				(+)
ESTs, Weakly similar to TYROSINE-PROTEIN KISE JAK3 (M.musculus)		(-)				
eukaryotic translation initiation factor 4, gamma 2	EIF4G2	(+)	(+)	RCC	C	
ribosomal protein S7	RPS7	(+)				
acidic ribosomal phosphoprotein PO	RPLP0	(+)	(+)	RCC	C	(+)
ribosomal protein S5	RPS5	(+)				
guanine nucleotide binding protein, beta 2, related sequence 1	GNB2L1	(+)	(+)	RCC	C	
meprin 1 alpha	MEP1A	(-)	(+)	RCC	DC	
aldo-keto reductase family 1, member B8 (Fgfrp) fibroblast growth factor regulated protein)	AKR1B10	(+)				
phosphoprotein enriched in astrocytes 15	PEA15	(+)	(+)	RCC	C	(+)
RIKEN cD 2600017H24 gene		(+)				
cytochrome c oxidase, subunit VIc	COX6C	(-)	(+)	RCC	DC	
interferon gamma receptor	IFNGR1	(+)	(+)	RCC	C	(+)
ADP-ribosyltransferase (D+)	ADPRTL2	(+)				
D-dopachrome tautomerase	DDT	(-)	(-)	RCC	C	
annexin A2	ANXA2	(+)	(-)(+)	RCC	conflict	
expressed sequence A1852479	CDKL3	(-)				
ribosomal protein L6	RPL6	(+)	(+)	RCC	C	
solute carrier family 22 (organic cation transporter), member 1	SLC22A1	(-)	(+)	RCC	DC	
platelet-activating factor acetylhydrolase, isoform 1b, alpha1 subunit	PAFAH1B3	(+)				
inosine 5'-phosphate dehydrogenase 2	IMPDH2	(+)				
elastin, light polypeptide (Lca)	CLTA	(+)				
cystatin B	CSTB	(+)				
pre B-cell leukemia transcription factor 1	PBX1	(-)				

annexin A4	ANXA4	(+)	(+)	RCC	C	(+)
small proline-rich protein 1A	SPRR1A	(+)				
chemokine (C-C) receptor 2	CCR2	(+)	(+)	RCC	C	
nucleophosmin 1	NPM1	(+)	(+)	RCC	C	
solute carrier family 15 (H <sup>+</sup> /peptide transporter), member 2	SLC15A2	(-)				
CD24a antigen	CD24	(+)	(+)	RCC	C	
ribosomal protein S15	RPS15	(+)				
ribosomal protein S15	SYN1	(+)				
Mus musculus, clone MGC36997 IMAGE:4948448, mR, complete cds	MGC36997	(+)				
tropomyosin 2, beta	TPM2	(+)				
prion protein	PRNP	(-)				
klotho	KL	(-)	(-)	RCC	C	
serine palmitoyltransferase, long chain base subunit 1	SPTLC1	(-)	(+)	RCC	DC	
chemokine orphan receptor 1	RDC1	(+)				
S100 calcium binding protein A13	S100A13	(+)				
RIKEN cD 1500010B24 gene	EIF1A	(+)	(+)	RCC	C	(+)
calpain, small subunit 1	CAPNS1	(-)	(+)	RCC	DC	
Ngf-A binding protein 2	NAB2	(+)				
ribonucleotide reductase M1	RRM1	(-)	(+)	RCC	DC	
sulfotransferase-related protein SULT-X1	Sult-x1	(+)				
4-hydroxyphenylpyruvic acid dioxygenase	HPD	(-)	(-)	RCC	C	
peroxiredoxin 5	PRDX5	(+)	(?)	RCC	conflict	
ribosomal protein S4, X-linked	RPS4X	(+)				(+)
solute carrier family 27 (fatty acid transporter), member 2	SLC27A2	(-)				
isovaleryl coenzyme A dehydrogenase	IVD	(-)				
thymoma viral proto-oncogene 1	AKT1	(+)	(+)	RCC	C	
protein tyrosine phosphatase, non-receptor type 9	PTPN9	(+)				
SAR1a gene homolog (S. cerevisiae)	SAR1	(+)	(-)	RCC	DC	
eukaryotic translation initiation factor 4E binding protein 1	EIF4EBP1	(+)				
RIKEN cD 4921537D05 gene	NY-REN-58	(+)				
transcription elongation regulator 1 (CA150)	TCERG1	(+)				
keratin complex 2, basic, gene 8	KRT8	(+)	(+)	RCC	C	
ESTs, Weakly similar to Jc7182 +/- dependent vitamin C (H.sapiens)	SLC23A3	(-)				
amine N-sulfotransferase	Sultn	(-)				
ADP-ribosylation factor 1	ARF1	(+)				
cyclin-dependent kinase 4	CDK4	(+)				(-)
ras homolog B (RhoB)	ARHB	(+)	(+)	RCC	C	

calbindin-D9K	CALB3	(-)				
baculoviral IAP repeat-containing 1a	BIRC1	(+)				
ESTs, Weakly similar to TYROSINE-PROTEIN KISE JAK3 (M.musculus)	C1QR1	(+)				
apoptosis inhibitory protein 5	API5	(+)				
spectrin SH3 domain binding protein 1	SSH3BP1	(+)				
ribosomal protein S3a	RPS3A	(+)	(+)	RCC	C	
calpain 2	CAPN2	(+)				
ribosomal protein L12	RPL12	(+)	(+)	RCC	C	(+)
ribosomal protein S16	RPS16	(+)	(+)	RCC	C	
Ia-associated invariant chain expressed sequence AI413331	CD74	(+)	(+)	RCC	C	
glucose regulated protein, 58 kDa	GRP58	(+)	(+)	RCC	C	
amiloride binding protein 1 (amine oxidase, copper-containing)	ABP1	(+)	(+)	RCC	C	
ESTs, Weakly similar to YMP2- CAEEL. HYPOTHETICAL 30.3 KD PROTEIN B0361.2 IN CHROMOSOME III (C.elegans)	3230401L03Rik	(+)				
annexin A3	ANXA3	(+)				
dolichyl-di-phosphooligosaccharide- protein glycotransferase	DDOST	(+)				
anterior gradient 2 (Xenopus laevis)	AGR2	(-)				
T-box 6	TBX6	(+)				
procollagen, type V, alpha 1	COL5A1	(+)	(+)	RCC	C	(+)
D segment, Chr 17, human D6S56E 2	LSM2	(+)				
cellular nucleic acid binding protein	ZNF9	(+)	(+)	RCC	C	
claudin 4	CLDN4	(+)				
fibrillin 1	FBN1	(+)				
ubiquitin-like 1	UBL1	(+)	(+)	RCC	C	(+)
period homolog 1 (Drosophila)	PER1	(-)				
procollagen, type IV, alpha 1	COL4A1	(+)	(+)	RCC	C	
protein phosphatase 2a, catalytic subunit, beta isoform	PPP2CB	(+)	(-)	RCC	DC	
Fas apoptotic inhibitory molecule	FAIM	(+)				
ESTs	FLJ23447	(-)				
breakpoint cluster region protein 1	BANF1	(+)				
RAN, member RAS oncogene family	RAN	(+)	(+)	RCC	C	
src-like adaptor protein	SLA	(+)				(+)
A kinase (PRKA) anchor protein 2	AKAP2	(+)	(-)	RCC	DC	
Unknown		(-)				
serine/threonine protein kinase CISK	SGKL	(+)				

D methyltransferase (cytosine-5) 1	DNMT1	(+)				(+)
proteasome (prosome, macropain) subunit, beta type 10	PSMB10	(+)	(+)	RCC	C	(+)
lymphocyte antigen 6 complex, locus E	LY6E	(+)				
colony stimulating factor 1 (macrophage)	CSF1	(+)	(+)	RCC	C	
procollagen lysine, 2-oxoglutarate 5-dioxygenase 2	PLOD2	(+)	(+)	RCC	C	(+)
upstream transcription factor 1	USF1	(-)				
ESTs, Moderately similar to T46312 hypothetical protein DKFZp434J111.1 (H.sapiens)		(+)				
magoh-shi homolog, proliferation-associated (Drosophila)	MAGOH	(+)	(+)	RCC	C	
TG interacting factor	TGIF	(+)	(+)	RCC	C	(+)
lymphocyte antigen 6 complex, locus A	LY6H	(+)				
non-catalytic region of tyrosine kinase adaptor protein 1	NCK1	(+)	(+)	RCC	C	
tissue inhibitor of metalloproteinase	TIMP1	(+)	(+)	RCC	C	(+)
proteasome (prosome, macropain) 28 subunit, alpha	PSME1	(+)				
sigl sequence receptor, delta	SSR4	(+)	(+)	RCC	C	
ESTs, Highly similar to organic cation transporter-like protein 2 (M.musculus)		(-)				
ESTs		(-)				
pyruvate kinase liver and red blood cell	PKLR	(-)	(-)	RCC	C	
acyl-Coenzyme A oxidase 1, palmitoyl	ACOX1	(-)	(+)	RCC	DC	
CD59a antigen	CD59	(-)	(+)	RCC	DC	(+)
period homolog 2 (Drosophila)	PER2	(-)				
peroxisomal sarcosine oxidase	PIPOX	(-)	(-)	RCC	C	
RIKEN cD 2810418N01 gene	KIAA0186	(+)				
1-acylglycerol-3-phosphate O-acyltransferase 3; expressed sequence AW493985	AGPAT3	(-)	(-)	RCC	C	
ESTs		(-)				
cholinergic receptor, nicotinic, beta polypeptide 1 (muscle)	CHRNB1	(+)				
ESTs		(-)				
adenylyl cyclase-associated CAP protein homolog 1 (S. cerevisiae, S. pombe)	CAP	(+)				
thiamin pyrophosphokinase	TPK1	(-)				
myocyte enhancer factor 2A	MEF2A	(+)	(+)(-)	RCC	conflict	
ESTs, Weakly similar to limb expression 1 homolog (chicken) (Mus musculus) (M.musculus)		(+)				
tolll-like receptor 2	TLR2	(+)				

small inducible cytokine B subfamily (Cys-X-Cys), member 10	SCYB10	(+)				
ESTs		(-)				
glycerol-3-phosphate acyltransferase, mitochondrial	GPAT	(-)				
retinoic acid early transcript gamma	ULBP2	(+)				
mammary tumor integration site 6	EIF3S6	(+)	(+)	RCC	C	
CD72 antigen	CD72	(+)				
RAR-related orphan receptor alpha	RORA	(-)				
testis derived transcript	TES	(+)	(+)	RCC	C	(+)
ESTs		(+)				
a disintegrin-like and metalloprotease (repolydin type) with thrombospondin type 1 motif, 2	ADAMTS2	(+)				
interleukin 1 receptor, type 1	IL1R1	(+)				
ESTs		(+)				
D methyltransferase 3B	DNMT3B	(+)				
RIKEN cD 2610524G09 gene	IER5	(+)				
Mus musculus, Similar to hypothetical protein FLJ20245, clone MGC:7940 IMAGE:3584061, mR, complete cds	FLJ20245	(+)				
high mobility group nucleosomal binding domain 2	HMG2	(+)	(+)	ROC	C	
crystallin, mu	CRYM	(+)	(-)	RCC	DC	
H2A histone family, member Z	H2AFZ	(+)	(+)	RCC	C	
transcription factor Dp 1	TFDP1	(+)	(+)	RCC	C	
microtubule associated testis specific serine/threonine protein kisc	MAST205	(+)				
cathepsin L	CTSL	(+)				(+)
kidney-derived aspartic protease-like protein	NAP1	(-)				
interferon-induced protein with tetratricopeptide repeats 3	IFT3	(+)				
sphingomyelin phosphodiesterase 2, neutral	SMPD2	(-)				
growth arrest and D-damage-inducible 45 gamma	GADD45G	(-)	(+)	RCC	DC	
vasodilator-stimulated phosphoprotein	VASP	(+)				
flavin containing monooxygenase 1	FMO1	(-)	(-)	RCC	C	
CD38 antigen	CD38	(+)				
tescin C	TNC	(+)				

Table 10

	Ontology	Early (A)				
	Category	Average Expression	Average Expression UP	Number Genes UP	Average Expression DOWN	Number Genes DOWN
Early (A)	oxidative phosphorylation	-0.418	0	0	-1.67	4
	DNA replication initiation	0.692	3.46	5	0	0
	DNA dependent DNA replication	0.461	4.86	9	-0.25	1
	regulation of translation	0.003	1.33	4	-1.31	3
	group transfer coenzyme metabolism	-0.452	0	0	-2.26	5
	ribonucleoside triphosphate biosynthesis	-0.256	0.41	1	-1.69	4
	purine nucleoside triphosphate biosynthesis	-0.256	0.41	1	-1.69	4
	purine ribonucleoside triphosphate biosynthesis	-0.256	0.41	1	-1.69	4
	glycolysis	-0.163	0.85	2	-2.15	6
	nucleoside triphosphate metabolism	-0.112	1.02	2	-1.69	4
	glucose metabolism	-0.347	0.85	2	-5.01	10
	hexose catabolism	-0.163	0.85	2	-2.15	6
	glucose catabolism	-0.163	0.85	2	-2.15	6
	alcohol catabolism	-0.163	0.85	2	-2.15	6
	monosaccharide catabolism	-0.163	0.85	2	-2.15	6
	monosaccharide metabolism	-0.376	0.85	2	-5.74	11
	purine ribonucleotide biosynthesis	-0.108	1.04	2	-1.69	4
	hexose metabolism	-0.347	0.85	2	-5.01	10
	carbohydrate catabolism	-0.163	0.85	2	-2.15	6
	S phase of mitotic cell cycle	0.389	6.14	12	-0.7	2
	DNA replication	0.389	6.14	12	-0.7	2
	main pathways of carbohydrate metabolism	-0.225	0.85	2	-3.1	8
	energy derivation by oxidation of organic compounds	-0.310	1.41	3	-5.44	10
	DNA replication and chromosome cycle	0.382	6.43	13	-0.7	2
	energy pathways	-0.353	1.41	3	-6.71	12
mitotic cell cycle	0.459	13.32	24	-0.93	3	
alcohol metabolism	-0.341	1.19	3	-6.65	13	

DNA metabolism	0.388	16.14	31	-2.19	5
carbohydrate metabolism	-0.256	3.12	8	-9.27	16
cell cycle	0.437	19.95	39	-1.15	4
cell proliferation	0.391	26.07	49	-3.79	8
cell growth and/or maintenance	0.108	49.42	96	-32.32	62
metabolism	0.092	73.79	156	-50.72	94
proton-transporting two-sector ATPase complex	-0.423	0	0	-1.69	4
hydrogen-translocating F-type ATPase complex	-0.423	0	0	-1.69	4
inner membrane	-0.387	0.64	2	-5.67	11
mitochondrial inner membrane	-0.371	0.64	2	-4.72	9
extrachromosomal DNA	-0.194	1.97	5	-4.49	8
extrachromosomal circular DNA	-0.194	1.97	5	-4.49	8
cytoplasm	0.059	56.82	118	-44.87	84
intracellular	0.110	85.21	179	-54.11	105
ATP-binding and phosphorylation-dependent chloride channel activity	-0.477	0	0	-1.43	3
intramolecular isomerase activity, transposing C=C bonds	-0.724	0	0	-3.62	5
cyclophilin-type peptidyl-prolyl cis-trans isomerase activity	0.336	1.9	4	-0.22	1
cis-trans isomerase activity	0.170	1.9	4	-0.88	2
peptidyl-prolyl cis-trans isomerase activity	0.336	1.9	4	-0.22	1
intramolecular isomerase activity	-0.533	0.42	1	-3.62	5
growth factor binding	-0.453	0.38	1	-3.1	5
transferase activity, transferring alkyl or aryl (other than methyl) groups	0.031	2	4	-1.78	3
lyase activity	-0.218	2.48	5	-5.75	10
isomerase activity	-0.217	2.32	5	-5.57	10
hydrogen ion transporter activity	-0.441	0	0	-4.41	10
magnesium ion binding	-0.199	1.06	2	-3.05	8
monovalent inorganic cation transporter activity	-0.441	0	0	-4.41	10

Early(A) and again in Early & Late (*)	carrier activity	-0.326	3.6	7	-12.73	21
	catalytic activity	0.017	51.13	112	-47.73	92
	fatty acid metabolism	-0.550	0.74	2	-6.24	8
	carboxylic acid metabolism	-0.524	1.36	4	-12.37	17
	organic acid metabolism	-0.524	1.36	4	-12.37	17
	biosynthesis	0.051	15.77	30	-13.07	23
	physiological processes	0.099	108.2	218	-73.12	138
	mitochondrion	-0.393	2.98	8	-19.88	35
	cytosol	0.340	10.55	21	-2.05	4
	oxidoreductase activity	-0.377	4.45	9	-17.66	26

	Ontology Category	Late (B)				
		Average Expression	Average Expression UP	Number Genes UP	Average Expression DOWN	Number Genes DOWN
Late (B)	urea cycle intermediate metabolism	0.243	1.13	2	-0.4	1
	antigen presentation\, endogeNumberus antigen	0.767	2.3	3	0	0
	antigen processing\, endogeNumberus antigen via MHC class I	0.767	2.3	3	0	0
	antigen presentation	1.123	6.74	6	0	0
	antigen processing	1.123	6.74	6	0	0
	immune response	0.842	24.77	24	-2.03	3
	response to wounding	0.384	5.53	8	-1.69	2
	response to pest/pathogen/parasite	0.791	13.56	13	-1.69	2
	catabolism	0.526	16.21	25	-1.48	3
	proteasome core complex (sensu Eukarya)	0.595	2.38	4	0	0
	microfibril	1.296	9.07	7	0	0
	extracellular matrix	0.963	17.34	18	0	0
	MHC class I receptor activity	0.767	2.3	3	0	0
	collagenase activity	0.877	2.63	3	0	0
	phospholipase inhibitor activity	0.897	2.69	3	0	0
	hydrolase activity\, acting on carbon-nitrogen (but Numbert peptide) bonds\, in linear amides	0.517	1.55	3	0	0
	apoptosis inhibitor activity	0.486	2.43	5	0	0
	hydrolase activity\, acting on carbon-nitrogen (but Numbert peptide) bonds	0.483	2.9	6	0	0
	transmembrane receptor activity	0.622	16.24	21	-1.31	3
	peptidase activity	0.464	10.75	19	-1.01	2
	receptor activity	0.513	20.32	30	-2.36	5



	<u>signal transducer activity</u>	0.395	26.85	42	-5.89	11
Late(B)	<u>defense response</u>	0.849	26.64	26	-2.03	3
and again in	<u>response to biotic stimulus</u>	0.796	27.26	27	-2.57	4
Early &	<u>response to external stimulus</u>	0.627	27.6	28	-5.02	8
Late (*)	<u>extracellular space</u>	0.664	53.03	64	-5.25	8

	Ontology Category	Continues (*)				
		Average Expression	Average Expression UP	Number Genes UP	Average Expression DOWN	Number Genes DOWN
Late(B)	<u>defense response</u>	0.696	16.7	24	0	0
and again in	<u>response to biotic stimulus</u>	0.523	16.7	24	-2.57	3
Early &	<u>response to external stimulus</u>	0.438	20.77	29	-5.02	7
Late (*)	<u>extracellular space</u>	0.247	39.54	49	-21.77	23
	<u>phenylalanine metabolism</u>	-1.203	0	0	-3.61	3
Early &	<u>phenylalanine catabolism</u>	-1.203	0	0	-3.61	3
Late (*)	<u>aromatic amiNumber acid family catabolism</u>	-1.203	0	0	-3.61	3
	<u>amiNumber acid catabolism</u>	-1.036	0	0	-5.18	5
	<u>amine catabolism</u>	-1.036	0	0	-5.18	5
	<u>amiNumber acid biosynthesis</u>	-0.873	0	0	-3.49	4
	<u>ribosome biogenesis</u>	0.872	8.72	10	0	0
	<u>ribosome biogenesis and assembly</u>	0.872	8.72	10	0	0
	<u>iNumberrganic anion transport</u>	0.282	2.54	3	-1.13	2
	<u>aromatic compound metabolism</u>	-0.366	2.14	2	-4.7	5
	<u>posttranslational membrane targeting</u>	-0.049	2.62	4	-2.96	3
	<u>blood coagulation</u>	0.340	3.86	5	-1.48	2
	<u>anion transport</u>	-0.034	2.54	3	-2.78	4
	<u>hemostasis</u>	0.340	3.86	5	-1.48	2
	<u>ER organization and biogenesis</u>	-0.049	2.62	4	-2.96	3
	<u>protein-ER targeting</u>	-0.049	2.62	4	-2.96	3
	<u>protein-membrane targeting</u>	-0.049	2.62	4	-2.96	3
	<u>amiNumber acid metabolism</u>	-0.721	0.54	1	-7.03	8
	<u>amiNumber acid and derivative metabolism</u>	-0.782	0.54	1	-9.14	10
	<u>response to chemical substance</u>	0.564	6.12	8	-1.04	1
	<u>amine metabolism</u>	-0.782	0.54	1	-9.14	10
	<u>response to abiotic stimulus</u>	0.435	8.97	11	-2.45	4
	<u>cytoplasm organization and biogenesis</u>	0.543	20.91	26	-4.07	5
	<u>macromolecule biosynthesis</u>	0.771	16.2	21	0	0
	<u>protein biosynthesis</u>	0.771	16.2	21	0	0
	<u>cell organization and biogenesis</u>	0.551	23.9	31	-4.07	5

<u>organelle organization and biogenesis</u>	0.387	12.19	16	-4.07	5
<u>cytosolic ribosome (sensu Eukarya)</u>	0.823	9.87	12	0	0
<u>eukaryotic 48S initiation complex</u>	0.750	3	4	0	0
<u>cytosolic small ribosomal subunit (sensu Eukarya)</u>	0.750	3	4	0	0
<u>eukaryotic 43S pre-initiation complex</u>	0.688	3.44	5	0	0
<u>small ribosomal subunit</u>	0.746	3.73	5	0	0
<u>actin filament</u>	0.340	2.02	3	-0.66	1
<u>ribosome</u>	0.786	16.5	21	0	0
<u>ribonucleoprotein complex</u>	0.763	19.07	25	0	0
<u>extracellular</u>	0.282	43.51	54	-21.77	23
<u>immunoglobulin binding</u>	1.103	3.31	3	0	0
<u>anion transporter activity</u>	-0.384	0.86	1	-2.78	4
<u>structural constituent of ribosome</u>	0.798	15.96	20	0	0
<u>chemokine activity</u>	0.902	4.51	5	0	0
<u>G-protein-coupled receptor binding</u>	0.902	4.51	5	0	0
<u>chemokine receptor binding</u>	0.902	4.51	5	0	0
<u>chemoattractant activity</u>	0.902	4.51	5	0	0
<u>actin binding</u>	0.176	4.89	8	-2.95	3
<u>structural constituent of cytoskeleton</u>	0.968	7.74	8	0	0
<u>structural molecule activity</u>	0.842	32	38	0	0
<u>ion transporter activity</u>	-0.562	1.42	2	-8.16	10
<u>RNA binding</u>	0.605	13.09	17	-1.59	2
Experiment Cons.	70% up 30% dn				

Table 11

Concordance / Disconcordance	Category	Size (Number of genes annotated to it by GO)	Concordance					Enrichment
			Average Expression	Average Expression UP	Number of Genes- UP	Average Expression Down	Number of Genes- DOWN	
Concordance	inmuNumberglobulin binding	6	1.103	3.31	3	0	0	0.034139907
	selenium binding	15	-0.388	0.46	1	-2.01	3	0.03816803
	extracellular matrix structural component conferring tensile strength activity	19	0.886	4.43	5	0	0	0.014124581
	structural constituent of ribosome	97	0.737	16.94	23	0	0	1.74394E-09
	extracellular matrix structural component	39	0.802	4.81	6	0	0	0.046877828
	RNA binding	207	0.563	16.21	27	-0.44	1	4.8428E-06
	structural molecule activity	321	0.761	29.76	37	-0.85	1	1.64291E-06
	cell adhesion molecule activity	124	0.458	7.19	11	-1.24	2	0.023941119
	nucleic acid binding	1059	0.502	36.8	64	-2.68	4	0.028128737
	cytosolic ribosome (sensu Eukarya)	27	0.730	8.03	11	0	0	3.54156E-07
	proteasome core complex (sensu Eukarya)	14	0.563	2.25	4	0	0	0.030644703
	eukaryotic 43S pre-initiation complex	15	0.525	2.1	4	0	0	0.036912006
	collagen	20	0.886	4.43	5	0	0	0.016227565
	small ribosomal subunit	20	0.698	3.49	5	0	0	0.016227565
	proteasome complex (sensu Eukarya)	24	0.520	2.6	5	0	0	0.034066018
	microfibril	36	1.029	7.2	7	0	0	0.008478551
Disconcordance	ribosome	122	0.737	16.94	23	0	0	1.7058E-07
	basement membrane	27	0.804	4.02	5	0	0	0.044662498
	ribonucleoprotein complex	186	0.701	20.34	29	0	0	1.18392E-07
	proton	193	0.601	14.42	21	-0.59	2	0.000240127
	extracellular matrix	156	0.873	14.36	15	-0.39	1	0.0116109

phenylalanine metabolism	4	-1.203	0	0	-3.61	3	0.014752454	14.52356557
phenylalanine catabolism	4	-1.203	0	0	-3.61	3	0.014752454	14.52356557
tyrosine metabolism	5	-1.033	0	0	-3.1	3	0.02375814	11.61885246
aromatic amino acid family catabolism	5	-1.203	0	0	-3.61	3	0.02375814	11.61885246
aromatic amino acid family metabolism	9	-1.038	0	0	-4.15	4	0.008957	8.606557377
DNA replication initiation	10	0.688	2.75	4	0	0	0.012315375	7.745901639
regulation of translation	22	0.135	1.88	4	-1.07	2	0.004420544	5.281296572
ribosome biogenesis	40	0.750	7.5	10	0	0	0.000145834	4.841188525
ribosome biogenesis and assembly	41	0.750	7.5	10	0	0	0.000178594	4.723110756
DNA dependent DNA replication	25	0.596	2.98	5	0	0	0.036826074	3.87295082
aromatic compound metabolism	36	-0.503	1.6	1	-5.12	6	0.00924943	3.765368832
posttranslational membrane targeting	39	0.491	4.71	5	-1.27	2	0.013591927	3.475725095
cell ion homeostasis	28	-0.506	0.55	1	-3.08	4	0.052913392	3.457991803
PK organization and biogenesis	45	0.483	5.13	6	-1.27	2	0.007403407	3.442622951
protein-PR targeting	45	0.483	5.13	6	-1.27	2	0.007403407	3.442622951
protein-membrane targeting	45	0.491	4.71	5	-1.27	2	0.026288289	3.012295082
amino acid metabolism	59	-0.80	0	0	-6.4	8	0.030340957	2.625729369
macromolecule biosynthesis	210	0.608	18.1	26	-1.07	2	6.91018E-06	2.581967213
protein biosynthesis	210	0.608	18.1	26	-1.07	2	6.91018E-06	2.581967213
carboxylic acid metabolism	137	-0.547	0.9	2	-10.2	15	0.001399216	2.402925691
organic acid metabolism	138	-0.547	0.9	2	-10.2	15	0.001727238	2.385513186
cytoplasm organization and biogenesis	290	0.656	21.32	25	-2.29	4	0.000779106	1.93647541
cell organization and biogenesis	378	0.634	25.11	32	-2.29	4	0.00037247	1.844262295
biogenesis	413	0.360	19.82	30	-5.79	9	0.000231323	1.828632954
death	167	0.523	9.6	13	-1.75	2	0.047103405	1.79349171
cell adhesion	224	0.609	13.41	18	-1.24	2	0.020497695	1.728995902
immune response	212	0.994	17.9	18	0	0	0.04390246	1.644177235
defense response	271	0.895	20.58	23	0	0	0.020890908	1.643503115
response to biotic stimulus	295	0.877	21.04	24	0	0	0.02809496	1.575437622
response to external stimulus	395	0.803	23.64	28	-0.34	1	0.048231031	1.421716124

cell growth and/or maintenance	1518	0.309	49.2	74	-18.64	25	0.003473821	1.262918746
protein metabolism	1000	0.542	40.04	57	-4.84	8	0.027923077	1.258709016
cellular process	2484	0.342	72.57	111	-23.97	31	0.046010892	1.107002851
physiological processes	3887	0.342	110.01	162	-37.2	51	0.019791016	1.061150662
DiscConcordance	12							
insulin-like growth factor binding	13							
organic cation transporter activity	22							
growth factor binding	37							
heparin binding	43							
glycosaminoglycan binding	88							
cation transporter activity	1093							
extracellular space	17							
one-carbon compound metabolism	32							
angiogenesis	27							
regulation of cell growth	21							
actin cytoskeleton organization and	35							
biogenesis	39							
blood vessel development	24							
cell growth	91							
actin filament-based process	248							
enzyme linked receptor protein	429							
signaling pathway	458							
organelle organization and biogenesis	80% up							
organNumbergenesis	20% dn							
morphogenesis								
Experiment Cons.								
Discordance								
Average Expression	Number of Genes	Average Expression Down	Number of Genes	EASE	Enrichment			

0.088	1.74	2	-1.39	2	0.0006	21.94520548
-0.267	0.38	1	-1.18	2	0.0155	15.19283456
0.088	1.74	2	-1.39	2	0.004	11.97011208
0.102	2.31	3	-1.8	2	0.0021	8.896704924
0.102	2.31	3	-1.8	2	0.0037	7.655304237
-0.446	0.38	1	-2.61	4	0.0421	3.740660025
0.084	9.48	12	-7.47	12	0.0496	1.430619091
-0.517	0	0	-1.55	3	0.0269	11.42224013
0.390	2.53	3	-0.58	2	0.0013	10.11344178
0.088	1.74	2	-1.39	2	0.0076	9.589041096
0.177	0.88	2	-0.35	1	0.0399	9.246575342
0.390	2.53	3	-0.58	2	0.0018	9.246575342
-0.018	1.74	2	-1.83	3	0.0027	8.298208641
0.177	0.88	2	-0.35	1	0.0509	8.090733425
0.226	1.65	3	-0.52	2	0.0491	3.56375132
-0.216	1.43	3	-3.37	6	0.0336	2.348928414
0.248	5.92	7	-2.7	6	0.0272	1.96139477
0.248	5.92	7	-2.7	6	0.0422	1.837201651
64% up 36% dm						

Table 12

		Changed genes	Changed genes	P Value	Changed genes	P Value
1	All data	1325	N.A.		N.A.	
2	Both early & late time points (*)	323	93	0.0001	20	0.9438
3	Early time point (A)	629	114	0.0182	35	0.3757
4	Late time point (B)	373	71	0.3105	28	0.2972
5	Up regulated	802	209	<0.0001	30	<0.0001
6	Down regulated	523	69	<0.0001	53	<0.0001
7	Regeneration/ RCC: Concordant	278	278	0	0	<0.0001
8	Regeneration/ RCC: Disconcordant	83	.0	<0.0001	83	0
9	Rest of the Data	964	0	0	0	0
10	VHL pathway	104	59	0	16	0.0001
11	Hypoxia pathway	95	35	0.0001	16	<0.0001
12	HRE target (HIF)	17	4	0.968	7	<0.0001
13	IGF pathway	37	9	0.7628	8	0.0003
14	Myc pathway	136	55	<0.0001	10	0.714
15	p53 pathway	262	80	<0.0001	32	<0.0001
16	NF- $\kappa$ B pathway	52	19	0.0083	5	0.4681
17	pattern-1	225	32	0.0132	15	0.8808
18	pattern-2	192	57	0.0008	2	0.0021
19	pattern-3	51	10	0.9856	5	0.4331
20	pattern-4	37	13	0.0419	0	0.213
21	pattern-5	187	38	0.9708	8	0.3031
22	pattern-6	83	27	0.0075	7	0.531
23	pattern-7	18	3	0.9119	2	0.7092
24	pattern-8	136	27	0.9346	7	0.7165
25	pattern-9	10	1	0.6659	0	0.872
26	pattern-10	41	6	0.4547	5	0.2006
27	pattern-11	45	4	0.0759	9	0.0003
28	pattern-12	36	11	0.1906	0	0.223
29	pattern-13	3	0		0	
30	pattern-14	32	13	0.0083	0	0.2688
31	pattern-15	19	4	0.8219	2	0.7615
32	pattern-16	86	6	0.002	14	0.0001
33	pattern-17	6	0		0	
34	pattern-18	13	1	0.4216	2	0.4254
35	pattern-19	26	3	0.3697	0	0.3589
36	pattern-20	6	1		0	
37	pattern-21	2	0		0	
38	pattern-22	3	0		0	
39	pattern-23	6	2		1	
40	pattern-24	3	1		0	
41	pattern-25	1	0		0	
42	pattern-26	1	0		0	
43	pattern-27	1	0		0	

Changed genes	P Value	Changed genes	P Value	Changed genes	P Value
N.A.		N.A.		N.A.	
210	0.0004	323	0	0	0
480	0.0068	0	0	629	0
274	0.7706	0	0	0	0
563	0.0116	189	0.4317	336	<0.0001
401	0.0116	134	0.4317	293	<0.0001
0	0	93	0.0001	114	0.0182
0	0	20	0.9438	35	0.3757
964	0	210	0.0004	480	0.0068
29	0	28	0.6094	50	0.9788
44	<0.0001	24	0.9325	50	0.3478
6	0.0012	2	0.3499	12	0.0936
20	0.0162	10	0.852	19	0.7547
71	<0.0001	39	0.2596	61	0.5789
150	<0.0001	69	0.4568	112	0.1009
28	0.003	19	0.0549	21	0.3668
178	0.0362	96	<0.0001	122	0.1102
133	0.2018	109	0	76	0.005
36	0.7772	9	0.2583	39	0.0001
24	0.3239	6	0.268	31	<0.0001
141	0.5363	24	<0.0001	7	0
49	0.0036	29	0.0522	8	<0.0001
13	0.8685	0	0.0264	7	0.5211
102	0.7072	5	<0.0001	130	0
9	0.4006	3	0.9782	3	0.3681
30	0.8709	8	0.4873	1	<0.0001
32	0.8695	16	0.1545	23	0.9099
25	0.7358	9	0.8871	22	0.1989
3		0		0	
19	0.1098	6	0.5051	24	0.0054
13	0.8245	0	0.0217	19	<0.0001
66	0.5323	2	<0.0001	79	<0.0001
6		0		6	
10	0.9863	0	0.0729	0	0.001
23	0.1228	0	0.0054	17	0.1408
5		0		5	
2		0		0	
3		0		3	
3		0		0	
2		0		0	
1		0		1	
1		0		1	
1		0		0	
Changed genes	P Value	Changed genes	P Value	Changed genes	P Value
N.A.		N.A.		N.A.	



0	0	189	0.4317	134	0.4317
0	0	336	<0.0001	293	<0.0001
373	0	277	<0.0001	96	<0.0001
277	<0.0001	802	0	0	0
96	<0.0001	0	0	523	0
71	0.3105	209	<0.0001	69	<0.0001
28	0.2972	30	<0.0001	53	<0.0001
274	0.7706	563	0.0116	401	0.0116
26	0.5282	85	<0.0001	19	<0.0001
21	0.2144	63	0.2762	32	0.2762
3	0.4852	10	0.9163	7	0.9163
8	0.4775	25	0.4728	12	0.4728
36	0.7193	113	<0.0001	23	<0.0001
81	0.3009	199	<0.0001	63	<0.0001
12	0.5011	43	0.0014	9	0.0014
7	<0.0001	0	0	225	0
7	<0.0001	192	0	0	0
3	0.0018	0	0	51	0
0	0.0006	37	<0.0001	0	<0.0001
156	0	181	0	6	0
46	<0.0001	83	<0.0001	0	<0.0001
11	0.0012	11	0.9139	7	0.9139
1	<0.0001	135	0	1	0
4	0.4865	0	0.0004	10	0.0004
32	<0.0001	0	<0.0001	41	<0.0001
6	0.0843	0	<0.0001	45	<0.0001
5	0.155	36	<0.0001	0	<0.0001
3		0		3	
2	0.0203	32	<0.0001	0	<0.0001
0	0.0213	19	0.0007	0	0.0007
5	<0.0001	5	0	81	0
0		0		6	
13	<0.0001	0	<0.0001	13	<0.0001
9	0.3918	17	0.6832	9	0.6832
1		0		6	
2		1		1	
0		3		0	
6		0		6	
3		3		0	
0		1		0	
0		0		1	
1		0		1	

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Table 14

Ischemic	day 1	day 2	day 5	day 14	Cluster/ Trend	Title
1	0.9816	0.8677	0.8710	0.8696	1	potassium channel, subfamily K, member 2
2	0.9090	0.7764	0.6022	0.8083	1	ESTs
3	0.8806	0.5878	0.4266	0.6908	1	RIKEN cDNA 130000P22 gene
4	0.6697	0.7737	0.6545	0.6917	1	DNA segment, Chr 8, Brigham & Women's Genetics 1320 expressed
5	1.1098	0.8817	0.7895	0.8394	1	yolk sac gene 2
6	1.0931	0.8849	0.8035	0.9308	1	RIKEN cDNA 231067/B10 gene
7	0.8617	0.8261	0.5534	0.9308	1	stenoy-Coenzyme A deutanase 1
8	0.9097	0.6450	0.4066	0.4316	1	malonyl-CoA decarboxylase
9	1.0502	0.7381	0.5969	0.7172	1	Mus musculus ercrtin-2 (tcrd) cDNA, complete cds
10	0.8590	0.7195	0.6667	0.7828	1	beta2-galactosidase, clone 14
11	1.0703	0.8504	0.7747	0.8387	1	beta2-galactosidase, clone 14
12	0.9683	0.7420	0.6598	0.8185	1	beta2-galactosidase, clone 14
13	1.0738	0.8411	0.7532	0.8033	1	Unknown
14	0.7536	0.5918	0.5231	0.7251	1	ESTs
15	0.9743	0.7118	0.5901	0.8200	1	RIKEN cDNA 6430559E15 gene
16	0.9743	0.7476	0.6336	0.8197	1	canine palmitoyltransferase 1, muscle
17	1.2001	0.7899	0.7046	0.7625	1	protein C
18	0.9439	0.6887	0.3369	0.8669	1	RIKEN cDNA 1810036E22 gene
19	0.9697	0.5924	0.4049	0.4827	1	cartilage oligomeric matrix protein
20	0.9287	0.6604	0.6005	0.7432	1	reduced in osteosclerosis transporter
21	0.9338	0.9959	0.8186	0.6981	1	insulin-like growth factor binding protein 1
22	0.9549	0.6340	0.7963	0.6977	1	succinate dehydrogenase complex, subunit A, flavoprotein (Fp)
23	0.9978	0.6034	0.8285	0.7812	1	Mus musculus, similar to quinine rotenone-like protein, clone IMAGE:4977405, mRNA, partial cds
24	0.9025	0.6381	0.5777	0.7155	1	expressed sequence AB59121
25	1.0040	0.8389	0.9240	0.8771	1	cytochrome c oxidase, subunit VIIa.1
26	1.0503	0.8404	0.9240	0.8771	1	RNA polymerase II
27	1.0104	0.7286	0.6449	0.8329	1	RIKEN cDNA 2610007A16 gene
28	0.8252	0.6482	0.6632	0.9195	1	DNA segment, Chr 4, Wayne State University 125, expressed
29	0.8853	0.6853	0.8632	0.8311	1	betaine-homocysteine methyltransferase
30	1.1359	0.8853	0.9206	0.8311	1	phosphofructokinase, liver, B-type
31	1.1378	0.9208	0.9501	1.0013	1	RIKEN cDNA 9130022E05 gene
32	0.8210	0.4811	0.9501	1.0191	1	cytochrome P450, 2a4
33	1.0851	0.8315	0.4326	0.6001	1	spike center family 22 (organic cation transporter) like 2
34	1.0287	0.9225	0.7763	0.9361	1	expressed sequence AB15037
35	0.9210	0.7445	0.9075	1.0134	1	succinate-Coenzyme A lyase, ADP-forming, beta subunit
36	1.0434	0.7947	0.7575	0.8569	1	intercalin 11 receptor, alpha chain 1
37	0.8544	0.4981	0.8247	0.9446	1	prolactin receptor related sequence 1
38	0.8627	0.7794	0.4663	0.7053	1	retinoid-inducible tyrosine phosphatase 5
39	0.9799	0.5516	0.7622	0.8158	1	RIKEN cDNA 100531P gene
40	1.1516	0.5399	0.8120	0.6525	1	creatine kinase, brain
			0.7652	0.9257	1	

41	0.9616	0.4203	0.4189	0.6665	0.6330	1	deidunase, isodehydriase, type I
42	0.9403	0.6639	0.6705	0.7125	0.7930	1	Yin muscush, clone MCK-1942, complete cds, alternatively spliced
43	0.9686	0.6042	0.5819	0.6591	0.7671	1	H2A histone family member 2
44	0.8893	0.7417	0.7801	0.8417	0.7807	1	glycine aminotransferase (L-aminine:glycine aminotransferase)
45	0.9561	0.5715	0.5664	0.7305	0.5106	1	thyroid hormone responsive SPOT14 homolog (Rattus)
46	0.9350	0.8253	0.8458	0.9079	0.9736	1	ESTs
47	1.0782	0.8613	0.7499	0.8548	0.9499	1	expressed sequence C79732
48	1.0587	0.6923	0.6461	0.7430	0.8694	1	microtubule-associated protein tau
49	0.9518	0.7034	0.6747	0.7329	0.8453	1	methionyl-tRNA-Cysteine A mutase
50	0.9518	0.7034	0.6747	0.7329	0.8453	1	calbindin-28k
51	0.9378	0.6674	0.6524	0.7042	0.8523	1	Mus musculus, clone MCK-1942, complete cds
52	0.9378	0.6674	0.6524	0.7042	0.8523	1	Mus musculus, guanine nucleotide binding protein (G protein), gamma 5, clone MCK-1942
53	0.9370	0.5155	0.4658	0.5221	0.6916	1	IMAGE:591324, mRNA, complete cds
54	0.8953	0.6357	0.5800	0.6558	0.7498	1	ESTs
55	1.0914	0.9025	0.8354	0.9409	1.0999	1	Riken cDNA 120001SG03 gene
56	0.8811	0.5119	0.4372	0.6067	0.7780	1	Riken cDNA 120001HD15 gene
57	1.0235	0.8414	0.7692	0.8871	1.0112	1	ESTs, similar to 555310 hypothetical protein YPL1910 - yeast (Saccharomyces cerevisiae) (S.cerevisiae)
58	1.0699	0.8933	0.8374	0.9557	1.0522	1	phosphodiesterase 1A, calmodulin-dependent
59	1.1476	0.8228	0.7292	0.9278	1.1484	1	Riken cDNA 5730403B10 gene
60	0.8894	0.7555	0.7420	0.8056	0.8780	1	Mus musculus, similar to chromosome 20 open reading frame 36, clone IMAGE:5356821, mRNA, partial cds
61	1.0316	0.8506	0.8489	0.9242	1.0091	1	Riken cDNA 5330445015 gene
62	0.9716	0.8073	0.8032	0.8679	0.9415	1	Mus musculus, clone IMAGE:5667158, mRNA, partial cds
63	0.9313	0.7977	0.7945	0.8947	0.9574	1	expressed sequence AW140407
64	1.0649	0.988	0.8434	0.9302	1.1040	1	ESTs
65	0.9448	0.7713	0.8895	0.7771	1.0326	1	DnaJ (Hsp40) homolog, subfamily A, member 1
66	1.0821	0.7559	0.7927	0.9098	1.1743	1	solute carrier family 25 (mitochondrial deoxynucleotide carrier), member 19
67	0.9277	0.3999	0.4565	0.5864	0.8842	1	ESTs
68	0.7433	0.4332	0.4695	0.5011	0.7191	1	carboxylesterase 3
69	0.9209	0.4518	0.4165	0.6056	0.8343	1	borax-ATPase A dehydrogenase
70	1.0652	0.6909	0.7498	0.8254	1.0113	1	Ubr1
71	0.8915	0.4577	0.2289	0.3117	0.8163	1	Ubr1
72	0.8809	0.5080	0.3873	0.6599	0.8163	1	hydroxyglutaryl dehydrogenase-3, delta-S-3-beta
73	1.0907	0.7118	0.5112	0.6554	0.9502	1	expressed sequence AB775199
74	0.9767	0.7940	0.6455	0.8544	0.9603	1	expressed sequence AL018056
75	1.0843	0.5882	0.4355	0.4414	0.6802	1	aldolase protein I
76	0.9526	0.6696	0.6248	0.7803	0.9601	1	mitochondrial ribosomal protein L39
77	0.9184	0.6949	0.7318	0.7823	0.8023	1	Riken cDNA 9530038B02 gene
78	1.0714	0.6146	0.7393	0.7891	0.8486	1	expressed sequence AW493985
79	0.8850	0.3202	0.3907	0.4495	0.4816	1	cell death-inducing DNA fragmentation factor, alpha subunit-like effector B
80	0.7269	0.5453	0.6162	0.6336	0.7483	1	thiodiol S-methyltransferase
81	0.8850	0.5453	0.6162	0.6336	0.7483	1	solute carrier family 25 (mitochondrial carrier, adenine nucleotide translocator), member 10
82	1.1340	0.3775	0.4685	0.5637	0.7175	1	lecithinase
83	1.0887	0.6004	0.6693	0.7303	0.8260	1	Riken cDNA 2310009B04 gene

84	1.0659	0.7227	0.7162	0.8724	0.9555	1	RIKEN cDNA 101001M04 gene expressed sequence A1182362
85	0.9264	0.4762	0.4532	0.6724	0.7798	1	cytochrome P450, 2A10
86	1.0592	0.4925	0.4059	0.6877	0.8827	1	expressed sequence A1182362
87	1.0641	0.4867	0.3117	0.7157	0.8382	1	Mus musculus, Similar to retinol dehydrogenase type 6, clone MGC:25963 IMAGE3459862, mRNA, complete cds
88	0.9643	0.4328	0.4633	0.6991	0.7641	1	RIKEN cDNA 231002J220 gene
89	0.7675	0.3101	0.6495	0.9127	0.7127	1	ESTs, Moderately similar to S1207 hypothetical protein (N.musculus)
90	0.7815	0.3115	0.9148	0.6413	0.9727	1	DnaJ (Hsp40) homolog, subfamily B, member 12
91	0.8282	0.3113	0.6982	0.8583	0.8983	1	RIKEN cDNA 170003A24 gene
92	0.7941	0.3041	0.6592	0.8583	0.8983	1	lipoprotein lipase
93	0.7219	0.3133	0.3233	0.5017	0.6523	1	RIKEN cDNA 281047M14 gene
94	0.6989	0.3380	0.5438	0.6309	0.6902	1	ESTs
95	0.7982	0.7104	0.7488	0.8607	0.9440	1	peroxisomal membrane protein 2, 22 kDa
96	0.9605	0.6333	0.6775	0.8070	0.9296	1	muscle actin, isoform 2
97	0.8747	0.3931	0.4258	0.6434	0.7513	1	RIKEN cDNA 231000J20 gene
98	0.9680	0.7001	0.7289	0.8378	0.9105	1	Mus musculus mRNA for alpha-albumin protein
99	1.0413	0.5559	0.6532	0.8301	0.8800	1	theta containing monocysteine 1
100	0.8523	0.5420	0.6296	0.7517	0.7849	1	Mus musculus adult male liver cDNA, RIKEN full-length enriched library, clone 1300015B02:deoxyribonuclease II alpha, full insert sequence
101	1.0649	0.6761	0.7163	0.8861	0.8952	1	Kruppel-like factor 1 (cytoid)
102	0.9704	0.4594	0.6959	0.7039	0.7189	1	expressed sequence A1593249
103	0.8461	0.5762	0.6730	0.7503	0.7608	1	RIKEN cDNA 503142Z09 gene
104	0.8103	0.5746	0.3836	0.6615	0.6961	1	acetyl-Coenzyme A dehydrogenase, medium chain
105	1.0590	0.5318	0.5663	0.7909	0.7616	1	Mus musculus, Similar to hypothetical protein FJ10520, clone MGC:27885 IMAGE3497792, mRNA, complete cds
106	0.8183	0.6572	0.6766	0.7433	0.7375	1	expressed sequence A875557
107	1.0162	0.7861	0.9020	0.7655	0.8195	1	secreted and transmembrane 1
108	1.0282	0.4757	0.7437	0.4369	0.5688	1	diacylglycerol acyltransferase 1
109	1.0423	0.7559	0.8994	0.7359	0.8026	1	transmembrane protein
110	0.9604	0.5230	0.6123	0.3902	0.4596	1	transmembrane hydroxylase
111	1.0047	0.6246	0.7884	0.6474	0.7453	1	RIKEN cDNA 201002D11 gene
112	0.8286	0.5560	0.6649	0.5854	0.6333	1	ESTs, Weakly similar to AF182426.1 myristamide diacylase (R. norvegicus)
113	1.0706	0.5573	0.8174	0.6077	0.6430	1	sepiastin, lambda 1
114	0.9157	0.4763	0.6420	0.6277	0.6730	1	soluble carrier family 7 (cationic amino acid transporter, y+ system), member 9
115	1.0098	0.5704	0.6652	0.5633	0.7256	1	isovaleryl coenzyme A dehydrogenase
116	0.9352	0.5872	0.6652	0.6277	0.6430	1	lysine oxophthalate reductase, saccharinase dehydrogenase
117	0.8322	0.5872	0.6652	0.6277	0.6430	1	carbonic anhydrase 5, mitochondrial
118	0.8789	0.5839	0.6652	0.6277	0.6430	1	pancreatin
119	0.8789	0.5839	0.6652	0.6277	0.6430	1	calculation factor XIII, beta subunit
120	0.9066	0.5132	0.5815	0.5214	0.6715	1	serum phosphatidyl transferase 2
121	1.0286	0.5089	0.6087	0.5268	0.7038	1	expressed sequence A1593249
122	0.9886	0.6523	0.7070	0.6208	0.7805	1	Mus musculus, clone MGC:37818 IMAGE3508655, mRNA, complete cds
123	1.1261	0.5924	0.6651	0.5452	0.7937	1	muscle actin, isoform 2
124	0.9844	0.6231	0.7773	0.6301	0.7563	1	RIKEN cDNA 181002P18 gene
125	1.1712	0.5691	0.7058	0.5264	0.7447	1	lysine oxophthalate reductase, saccharinase dehydrogenase
126	0.9479	0.7389	0.7905	0.7286	0.8047	1	RIKEN cDNA 110038J12 gene

127	1.0157	0.4696	0.7027	0.4561	0.6971	1	J domain protein 1
128	0.9351	0.7323	0.8148	0.7266	0.8336	1	adducin 3 (gamma)
129	0.6681	0.6479	0.6819	0.6522	0.7914	1	phosphoryl-CoA hydroxylase
130	1.0525	0.8201	0.8350	0.8472	0.9659	1	Unknown
131	1.0470	0.3491	0.4474	0.4476	0.7893	1	protein phosphatase 1, regulatory (inhibitor) subunit 1A
132	0.8697	0.6571	0.6847	0.6817	0.7783	1	ESTs, weakly similar to ERK1 (Hs) sequence
133	0.9008	0.6215	0.6344	0.6362	0.7915	1	ESTs, weakly similar to ERK1 (Hs) sequence
134	1.0869	0.5833	0.7381	0.7338	0.8571	1	RIKEN cDNA 071008N11 gene
135	0.9425	0.6240	0.6233	0.6233	0.7877	1	RIKEN cDNA 2410021P16 gene
136	0.9033	0.6045	0.6401	0.6233	0.7390	1	endosomal growth factor
137	1.1972	0.6955	0.8314	0.8882	0.9795	1	Mut nucleolar. Similar to MIPPO5 protein, clone MGC:18783 IMAGE:418234, mRNA, complete cds
138	1.0090	0.7053	0.7495	0.7547	0.8487	1	enoyl Coenzyme A hydratase, short chain, 1, mitochondrial
139	1.0320	0.7674	0.8403	0.8382	0.9008	1	RIKEN cDNA 1300017C12 gene
140	0.6980	0.2962	0.3814	0.3800	0.4743	1	adenylate kinase 4
141	0.9453	0.5332	0.6121	0.6285	0.7339	1	transhyalase
142	0.9767	0.4281	0.4910	0.4584	0.5762	1	Proth
143	0.9457	0.5191	0.5988	0.5566	0.6680	1	catenulicoid pyrophosphatase-phosphodiesterase 2
144	0.8730	0.2441	0.3249	0.2815	0.4363	1	4-Hydroxyphenylpyruvate acid decarboxylase
145	0.9976	0.5594	0.6852	0.6182	0.7160	1	growth arrest specific 2, liver
146	0.9308	0.5770	0.6574	0.6105	0.6882	1	proteoglycan 2, liver
147	0.9990	0.6529	0.6922	0.6962	0.7626	1	transmembrane protein 8 (five membrane-spanning domains)
148	1.0217	0.6998	0.8362	0.8362	0.8390	1	transmembrane protein 8 (five membrane-spanning domains)
149	0.8990	0.5018	0.5856	0.5520	0.6361	1	transmembrane protein 8 (five membrane-spanning domains)
150	0.9146	0.5098	0.6191	0.6046	0.7392	1	transcription elongation factor A (SLD), 3
151	1.0865	0.4908	0.7191	0.6046	0.7392	1	transcription elongation factor A (SLD), 3
152	1.0318	0.5602	0.7579	0.7638	0.7638	1	transcription elongation factor A (SLD), 3
153	1.0318	0.5602	0.7579	0.7638	0.7638	1	transcription elongation factor A (SLD), 3
154	0.7704	0.1985	0.3914	0.2790	0.4076	1	folate receptor 1 (cdut)
155	0.8940	0.4600	0.5677	0.5110	0.6963	1	glucose-6-phosphatase, catalytic
156	0.9634	0.3947	0.7844	0.7270	0.8165	1	RIKEN cDNA G3056GB14 gene
157	1.0133	0.8106	0.7664	0.7576	0.6972	1	cytochrome P450, 3A5
158	0.8802	0.7198	0.5064	0.5414	0.4831	1	dehydrogenase
159	0.9990	0.6900	0.6239	0.6408	0.6133	1	gamma-glutamyl transpeptidase
160	1.0002	0.6882	0.6353	0.6282	0.6051	1	solute carrier family 22 (organic cation transporter), member 1
161	0.9077	0.7880	0.7017	0.7166	0.7518	1	acyltransferase, long-chain fatty acid
162	1.0057	0.7300	0.6902	0.6864	0.6660	1	acyltransferase, long-chain fatty acid
163	0.8681	0.7092	0.7332	0.7308	0.7308	1	ESTs
164	1.1117	0.5848	0.6594	0.6576	0.6527	1	RIKEN cDNA 130004C04 gene
165	1.0800	0.5603	0.5244	0.4742	0.5401	1	solute carrier family 22 (organic cation transporter), member 2
166	1.0942	0.5996	0.5594	0.5437	0.5630	1	transcobalamin 2
167	1.1004	0.7860	0.7853	0.7628	0.7845	1	transcobalamin 2
168	0.8939	0.3244	0.3173	0.2147	0.2562	1	transcobalamin 2
169	0.9275	0.4975	0.6047	0.5280	0.5993	1	ascorbate dehydrogenase 2 (NADPH), mitochondrial
170	1.0114	0.7205	0.7236	0.6446	0.7168	1	glutaryl-Coenzyme A dehydrogenase

171	1.0638	0.8670	0.8366	0.7863	0.8366	expressed sequence A W04-5660
172	1.0709	0.8877	0.8476	0.8111	0.8085	kinase insert domain protein receptor
173	0.8862	0.8522	0.8240	0.8077	0.8403	phosphoglycerate kinase 7
174	1.0240	0.6953	0.6481	0.7282	0.6652	ATPase family 13 (sodium-dependent dicarboxylate transporter), member 3
175	0.9576	0.7353	0.6591	0.7139	0.7480	ATPase family 13 (sodium-dependent dicarboxylate transporter), alpha subunit, isoform 1
176	1.2460	0.7445	0.3226	0.4247	0.7659	ATPase family 13 (sodium-dependent dicarboxylate transporter), alpha subunit, isoform 1
177	1.1002	0.6900	0.6302	0.6549	0.8531	ATPase family 13 (sodium-dependent dicarboxylate transporter), alpha subunit, isoform 1
178	1.1204	0.8348	0.7968	0.7543	0.5540	serologically defined colon cancer antigen 28
179	0.9352	0.8116	0.7968	0.7668	0.5540	proline dehydrogenase
180	0.9352	0.8116	0.7968	0.7668	0.5540	isoform 2 of proline dehydrogenase
181	1.0592	0.7760	0.7070	0.7888	0.7557	isoform 2 of proline dehydrogenase
182	1.3384	0.6018	0.4223	0.5567	0.5418	Unknown
183	1.0022	0.8612	0.6783	0.7359	0.8014	RIKEN cDNA 579040C10 gene
184	0.8546	0.7703	0.6541	0.6768	0.7313	ESTs
185	1.0201	0.8708	0.7479	0.7935	0.8518	ESTs, Weakly similar to TYROSINE-PROTEIN KINASE JAK3 (M. musculus)
186	0.9130	0.7572	0.7174	0.7053	0.7895	RIKEN cDNA 930631E13 gene
187	0.8750	0.6922	0.6513	0.6516	0.7287	ATP-binding cassette, anti-folate D (ALD), member 3
188	1.0250	0.7788	0.7025	0.7654	0.8268	ATP-binding cassette, anti-folate D (ALD), member 3
189	0.9676	0.7039	0.6232	0.6705	0.7215	ATP-binding cassette, anti-folate D (ALD), member 3
190	1.0332	0.6653	0.5330	0.5586	0.5527	ATP-binding cassette, anti-folate D (ALD), member 3
191	1.1325	0.6870	0.5330	0.5586	0.5527	ATP-binding cassette, anti-folate D (ALD), member 3
192	1.0245	0.8101	0.7693	0.8411	0.7119	Unknown
193	1.3776	0.4719	0.7015	0.5765	0.5463	citrate lyase beta like
194	0.9920	0.6257	0.7415	0.7693	0.6849	solute carrier family 34 (sodium phosphate), member 1
195	1.1545	0.7438	0.5510	0.6386	0.7072	Mus musculus, clone IMAGE-4974221, mRNA, partial cds
196	1.1146	0.8368	0.7779	0.8637	0.8170	heparin
197	1.2015	0.5233	0.3369	0.6275	0.5765	Mus musculus, clone IMAGE-3603661, mRNA, complete cds
198	1.0841	0.5163	0.5977	0.5704	0.6060	RIKEN cDNA 463240I08 gene
199	1.0379	0.6538	0.7209	0.7349	0.7375	giprolipase 1 (retal)
200	1.0144	0.6178	0.4537	0.6837	0.6640	D-glyceraldehyde 3-phosphate dehydrogenase
201	1.0144	0.6178	0.4537	0.6837	0.6640	Mus musculus, Similar to xylulokinase homology (H. influenzae), clone IMAGE-5043428, mRNA, partial cds
202	1.0332	0.4725	0.5407	0.6132	0.5781	Unknown
203	0.9993	0.7084	0.7611	0.7434	0.7461	Unknown
204	0.9764	0.6880	0.6602	0.6583	0.6583	ATP synthase, H <sup>+</sup> -transferring mitochondrial F1 complex, beta subunit
205	1.1638	0.598	0.5881	0.6376	0.7336	histidyl tRNA synthetase
206	0.9297	0.5303	0.5947	0.6322	0.5977	isolate carrier family 22 (organic cation transporter), member 1-like
207	0.9297	0.5303	0.5947	0.6322	0.5977	isolate carrier family 22 (organic cation transporter), member 1-like
208	1.0080	0.6441	0.7670	0.7477	0.7820	Rap1, GTPase-activating protein 1
209	1.0966	0.5961	0.6505	0.7207	0.7840	hemochromatosis 2, mitochondrial
210	1.1247	0.7141	0.7394	0.8393	0.8455	neprilysin alpha
211	0.9766	0.5290	0.3834	0.6728	0.6687	pyruvate dehydrogenase 2
212	1.0056	0.5933	0.6408	0.7343	0.7107	RIKEN cDNA 930552N12 gene
213	1.0585	0.7025	0.5965	0.7986	0.7874	malic enzyme, supernatant
214	1.0762	0.7857	0.7670	0.8569	0.8367	PPAR gamma coactivator-beta protein

215	0.9796	0.4365	0.4333	0.5143	0.6052	1	Kruppel-like factor 15	expressed sequence AW124722
216	1.1134	0.8427	0.8362	0.8630	0.8549	1	inositol polyphosphate-5-phosphatase, 75 kDa	
217	0.9568	0.6968	0.6821	0.6555	0.7712	1	RIKEN cDNA 579354006 gene	
218	0.9549	0.7735	0.7725	0.8198	0.8418	1	Unknown	
219	0.9852	0.7983	0.7732	0.8464	0.8625	1	Unknown	
220	0.9909	0.7662	0.7666	0.7394	0.7770	1	RIKEN cDNA 2310004102 gene	
221	0.9753	0.662	0.5830	0.5607	0.6293	1	Kruppel-like factor 9	ESTs, highly similar to arginine cation translocase protein 2 (M.musculus)
222	0.9656	0.7345	0.5801	0.6132	0.5488	1	brachyodan kinase A182934	ESTs, highly similar to arginine cation translocase E1, alpha polypeptide
223	0.9353	0.5803	0.5824	0.5344	0.5977	1	expressed sequence MGC-7898 IMAGE358217, mRNA, complete cds	
224	0.9697	0.6177	0.6167	0.6402	0.6521	1	Mus musculus, clone MGC-7898 IMAGE358217, mRNA, complete cds	
225	0.8572	0.3460	0.3796	0.3960	0.4323	1	human protein, p154	
226	0.9386	0.4639	0.4980	0.5248	0.5796	1	human protein, p154	
227	0.9386	0.4639	0.4980	0.5248	0.5796	1	Mus musculus, similar to ubiquitin-conjugating enzyme E2, variant 1, clone MGC/7660 IMAGE349088, mRNA, complete cds	
228	0.8769	0.6368	0.6346	0.6398	0.7097	1	expressed sequence AB30219	
229	1.0562	0.8293	0.7960	0.8341	0.8861	1	ESTs, weakly similar to YABs, YEAST HYPOTHETICAL 13.4 kD PROTEIN IN ACS1-CG3 INTERGENIC REGION (S.cerevisiae)	
230	1.1199	0.9255	0.9011	0.9208	0.9612	1	RIKEN cDNA 261026D03 gene	
231	1.1177	1.4144	1.3884	1.2935	1.2300	2	transforming growth factor beta 1 induced transcript 4	
232	0.8820	2.3168	1.6415	1.8457	1.2875	2	phospholipase A2, activating protein	
233	1.0149	2.3168	2.0042	1.2244	1.1310	2	coagulation factor III	
234	0.9157	2.3807	1.9796	1.9638	1.4305	2	WD repeat domain 1	
235	0.9157	1.4019	1.4473	1.4495	1.2616	2	Harvey rat sarcoma oncogene, subgroup B	
236	0.9033	1.6039	1.3419	1.3908	1.1307	2	acute carrier family 13 (cation/sulphate symporter), member 1	
237	0.8760	2.1221	1.5577	1.7149	1.3271	2	ESTs, mouse, clone MGC-18985 IMAGE401674, mRNA, complete cds	
238	0.8933	1.3513	1.1848	1.1199	1.2037	2	ESTs, mouse, clone MGC-18985 IMAGE401674, mRNA, complete cds	
239	1.0107	1.8379	1.5108	1.4259	1.2037	2	ESTs, mouse, clone MGC-18985 IMAGE401674, mRNA, complete cds	
240	1.1604	1.7770	1.5018	1.5037	1.3295	2	Trf receptor-associated factor 2	
241	0.9502	1.5740	1.2196	1.3172	1.182	2	growth differentiation factor 15	
242	1.0314	1.5023	1.2505	1.4018	1.3461	2	tumor necrosis factor receptor superfamily, member 1a	
243	0.9591	2.0042	1.3889	1.6818	1.3126	2	zinc finger protein 36, C3H type-like 1	
244	0.8665	1.5614	1.282	1.2877	1.5793	2	myelotomatois oncogene	
245	0.7701	1.9641	1.3653	1.5557	1.4424	2	a disintegrin-like and metalloprotease (regucalcin type) with thrombospondin type 1 motif, 1	
246	0.9626	1.4996	1.2622	1.5557	1.4424	2	catp2	
247	0.8347	2.6876	1.468	2.2063	1.8106	2	tensin C	
248	0.8995	1.4821	1.8892	2.0746	1.8274	2	phosphoprotein enriched in sarcoptes 15	
249	0.9244	2.2402	1.8668	1.8792	1.9387	2	cholesterol receptor, atoxoids, bean polyacrylate 1 (muscle)	
250	0.9244	2.2402	1.8668	1.8792	1.9387	2	cholesterol receptor, atoxoids, bean polyacrylate 1 (muscle)	
251	0.9493	1.3687	1.2938	1.3043	1.2955	2	elastin 7	
252	1.0134	1.6451	1.6312	1.5103	1.4454	2	EST, chicken-TNF-alpha factor	
253	0.9392	1.3161	1.2632	1.2824	1.2312	2	lyp1, catenase-like	
254	0.9216	2.0534	1.8881	1.8813	1.7964	2	RIKEN cDNA 110014003 gene	
255	0.8604	1.3457	1.2803	1.2674	1.2237	2	synanin B	
256	0.9198	1.4348	1.3808	1.4179	1.2070	2	intercellular adhesion molecule	
257	1.0637	2.2833	2.1868	2.1240	1.8610	2		
258	1.1002	1.6755	1.5558	1.6359	1.4731	2		



259	0.9795	1.3579	1.2472	1.2478	1.1988	2	ADP-ribosylator factor 1
260	0.9126	1.5544	1.3792	1.3364	1.3147	2	Mouse musculus, clone MGC29001 IMAGE3495957, mRNA, complete cds
261	1.1012	2.4132	2.0059	2.0296	1.6679	2	Mouse musculus, similar to trypsinogen 2, clone MGC3300 IMAGE2654381, mRNA, complete cds
262	0.8964	1.7022	1.5114	1.3836	1.5469	2	Bcl-2-interacting killer-like
263	1.1238	1.5098	1.4193	1.3938	1.3204	2	accessed sequences, C87272
264	0.9803	1.3292	1.3709	1.3531	1.3531	2	glucosylated-vascular 3-kinase, regulatory subunit, polypeptide 1 (p15 alpha)
265	0.8771	1.3645	1.3204	1.3038	1.3668	2	heat shock protein, 56 kDa 1
266	0.8771	1.3645	1.3204	1.3038	1.3668	2	heat shock protein, 56 kDa 1
267	0.8771	1.3645	1.3204	1.3038	1.3668	2	proteasome (prosome, macropain) subunit, alpha type 6
268	0.9063	1.5144	1.3115	1.1768	1.2713	2	RIKEN cDNA 110001224 gene
269	0.9063	1.5144	1.3115	1.1768	1.2713	2	MORF-related gene X
270	0.9085	1.9206	1.4645	1.2751	1.3404	2	Mouse musculus, similar to heterogeneous nuclear ribonucleoprotein A3 (H. sapiens), clone MGC37309 IMAGE4973085, mRNA, complete cds
271	0.8578	1.3028	1.1672	1.0462	1.2584	2	ADP-ribosyltransferase (NAD+ poly (ADP-ribose) polymerase) 2
272	0.8008	2.1114	1.8429	1.5531	1.6467	2	heat shock 70 kDa protein 4
273	1.0085	1.4867	1.3931	1.2873	1.3456	2	tumor-associated calcium signal transducer 2
274	1.0238	1.3838	1.2981	1.2238	1.2705	2	coagulation factor II (thrombin) receptor-like 1
275	0.8753	1.2512	1.1707	1.0575	1.1852	2	SH3 domain protein, domain 4 (microdomain)
276	0.9818	1.2473	1.1897	1.1530	1.1852	2	SH3 domain protein, domain 3
277	0.9810	1.2570	1.1916	1.1453	1.2259	2	SH3 domain protein complex AP-3, sigma 1 subunit
278	1.0146	1.4743	1.2704	1.2796	1.3323	2	RIKEN cDNA 120015A22 gene
279	0.9872	1.2897	1.1758	1.1738	1.2636	2	Mouse musculus, similar to connectin isoform B, clone MGC114474 IMAGE3981359, mRNA, complete cds
280	0.9331	1.6366	1.5384	1.2673	1.1768	2	RIKEN cDNA 130013G12 gene
281	1.0659	2.1308	2.0019	1.6135	1.5434	2	cyclin-dependent kinase 4
282	1.0657	1.9801	1.8893	1.5845	1.4756	2	tropomyosin 3, gamma
283	0.9989	3.9243	2.9267	2.1458	2.0938	2	fibroblast growth factor regulated protein
284	0.9859	4.6772	3.7273	2.5667	2.4503	2	kernin complex 2, basic, gene 8
285	0.9648	2.1187	2.1390	1.8064	1.7091	2	keratin complex 2, basic, gene 8
286	1.0154	1.5290	1.4963	1.3198	1.3474	2	serine (or cysteine) proteinase inhibitor, clade H (heat shock protein 47), member 1
287	1.0560	1.4037	1.3611	1.2613	1.2850	2	ubiquitin-conjugating enzyme E21
288	0.9310	1.2713	1.2741	1.0298	1.1224	2	neral proliferation, differentiation and control gene 1
289	0.9077	1.2020	1.1761	0.9695	1.0738	2	ORF-associated membrane protein 1
290	0.9077	1.2020	1.1761	0.9695	1.0738	2	salivary epylase-associated CAP protein homolog 1 (S. cerevisiae, S. pombe)
291	0.8963	1.2355	1.1705	1.1319	1.1040	2	proteasome (prosome, macropain) 26S subunit, non-ATPase, 10
292	1.1520	2.0319	1.9151	1.4794	1.5455	2	proteasome (prosome, macropain) 26S subunit, non-ATPase, 10
293	0.8870	1.2319	2.1131	1.4594	1.5706	2	varicella hemagglutinin
294	0.8870	1.2319	2.1131	1.4594	1.5706	2	glucanin 1
295	0.8438	1.2718	1.2777	1.0372	1.1603	2	phosco regulated protein, 58 kDa
296	0.8472	1.3494	1.3412	1.1025	1.1318	2	ESTs
297	0.9530	1.3953	1.4666	1.1966	1.3499	2	nitrogen activated protein kinase kinase kinase 1
298	1.0267	1.2245	1.2548	1.1265	1.1962	2	testis derived transcript
299	1.1267	2.3508	2.8522	1.9259	1.4845	2	expressed sequence BB120430
300	1.0701	1.3486	1.4268	1.1333	1.1333	2	actin, alpha 2, smooth muscle,orta
301	1.0242	1.3951	1.4901	1.3186	1.1331	2	transformation related protein 53
						2	TAF10 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 30 kDa

302	1.0327	5.978	6.2431	4.4856	2.3330	2	clutrin
303	1.3259	2.4505	2.5599	2.9061	1.7530	2	phosphatidylinositol 5H2-containing protein 3
304	0.9466	1.3646	1.4126	1.2605	1.1071	2	protein 2
305	1.2320	2.492	2.2419	1.9300	1.9962	2	serpin-like
306	1.0182	2.1818	2.2685	1.8189	1.3962	2	cofilin 1, non-muscle
307	0.9931	1.7838	1.9499	1.2777	1.3150	2	ribosomal protein L6
308	1.0653	1.3150	1.3859	1.2777	1.2402	2	ribosomal protein L21
309	1.8372	1.8475	1.6970	1.4678	1.3917	2	nas homolog B (RhoB)
310	1.8372	1.8475	1.6970	1.4678	1.3917	2	guanine nucleotide binding protein, beta 2, related sequence 1
311	1.0999	1.5457	1.6332	1.3656	1.3562	2	ribosomal protein S3
312	0.9765	1.2139	2.1961	1.4512	1.2718	2	RAN, member RAS oncogene family
313	1.5625	2.1075	2.0691	1.5412	1.2421	2	zinc finger protein 36, C3H type-like 2
314	1.0773	1.3922	1.4052	1.2814	1.1471	2	heparin binding epidermal growth factor-like growth factor
315	0.9822	1.6328	1.5965	1.3330	1.1288	2	myosin light chain, alkali, cardiac filament 1 homolog (S. cerevisiae)
316	0.9188	1.5654	1.5551	1.2580	1.0350	2	small chromosomal fraction 1
317	1.0793	5.5574	9.3127	3.9057	2.8346	2	SLD octanucleotide protein A6 (calyculin)
318	1.0126	1.6739	2.0456	1.5200	1.3133	2	ribosomal protein S3a
319	1.0942	1.7252	2.2267	1.5755	1.3133	2	ribosomal protein S3a
320	1.0637	1.8952	2.2258	1.8208	1.5419	2	ribosomal protein S3a
321	1.0565	1.1642	1.2306	1.2608	1.1147	2	RNA binding motif protein 3
322	1.0705	1.7679	1.9056	1.6945	1.5442	2	Mus musculus, clone MGC:46937 IMAGE:494848, mRNA, complete cds
323	0.9035	1.1975	1.2056	1.0761	1.0596	2	ribosomal protein S15
324	0.9085	1.3335	1.5674	1.2604	1.1466	2	laminin B1 subunit 1
325	0.9687	2.1927	3.3491	2.2394	1.8052	2	RIKEN cDNA 4933405C01 gene
326	0.9687	2.1927	3.3491	2.2394	1.8052	2	RIKEN cDNA 4933405C01 gene
327	0.9560	1.1802	1.1944	1.1540	1.3338	2	epidermal growth factor-containing fibulin-like extracellular matrix protein 2 expressed sequence AU015605
328	0.9764	1.7327	1.9320	1.6528	1.5458	2	PXYD domain-containing ion transport regulator 5
329	1.0645	1.4765	1.5744	1.4181	1.3466	2	uridine kinase plasmidogen activator receptor
330	1.0044	1.7007	1.8942	1.6124	1.3361	2	ribosomal protein L5
331	0.9628	1.4042	1.5318	1.3774	1.2929	2	thymoma viral protein-1
332	0.8445	1.5391	1.8649	1.4846	1.2736	2	interferon-induced protein with tetratricopeptide repeats 3
333	0.8871	1.5872	1.7722	1.5403	1.2828	2	interferon-induced protein with tetratricopeptide repeats 3
334	0.9141	2.0818	2.5152	2.0461	1.6516	2	interferon-induced protein with tetratricopeptide repeats 3
335	1.1017	2.0758	2.2732	2.2015	1.5380	2	human nuclear ribonucleoprotein A1
336	1.0187	2.3364	2.5172	2.3004	1.6877	2	ESTs, Weakly similar to YMP2, CAELI HYPOTHETICAL 30.3 KD PROTEIN BU361.2 IN
337	1.0187	2.3364	2.5172	2.3004	1.6877	2	chloride intracellular channel 1
338	1.0187	2.3364	2.5172	2.3004	1.6877	2	cytidine 5'-phosphatase synthase
339	1.0454	2.6605	2.8033	2.1381	1.8649	2	toluidin alpha 2
340	0.9616	4.1328	3.9255	2.9854	2.2979	2	auxilin A2
341	1.0485	5.5067	5.3463	4.4599	2.4356	2	auxilin A2
342	1.0107	1.6909	1.6517	1.5068	1.3155	2	transcription elongation factor 1 (CA150)
343	0.9674	1.1935	1.4909	1.3491	1.2548	2	ribosomal protein S6
344	0.9967	1.4998	2.2714	1.8420	1.6075	2	transcription elongation factor 1 (CA150)
345	0.9704	1.1767	1.4426	1.3022	1.2447	2	ribosomal protein S6
346	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
347	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
348	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
349	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
350	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
351	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
352	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
353	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
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357	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
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363	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
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418	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
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427	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
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437	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
438	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
439	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
440	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
441	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
442	0.9719	1.3444	1.6810	1.4334	1.4350	2	ribosomal protein S6
443	0.9719	1.3444	1.6810	1.433			

347	0.9439	2.1355	1.3845	1.2700	1.2523	2	E74-like factor 4 (see domain transcription factor)
348	0.9176	1.1151	1.2227	1.1718	1.1249	2	TAF12-like granule-associated RNA binding protein-like 1
349	0.9937	1.2217	1.3762	1.2781	1.2244	2	TAF12 RNA-binding protein II, TATA box binding protein (TBP)-associated factor, 32 kDa
350	1.0739	1.6211	1.9040	1.8066	1.7125	2	ribosomal protein L27e
351	1.1687	1.9215	2.4374	2.1935	1.7941	2	serine, beta, cytoplasmic
352	0.9678	2.1397	2.4859	1.9250	1.3770	2	serine, acidic, cytosolic rich glycoprotein
353	0.9362	1.3857	1.9035	1.8941	1.6016	2	ubiquitin-conjugating enzyme E2H
354	0.9229	1.1451	1.6329	1.3079	1.2103	2	expressed sequence AW146109
355	1.0529	1.6553	1.3525	1.3079	1.2103	2	a disintegrin and metalloproteinase domain 12 (metrin alpha)
356	1.1090	1.5553	1.4332	1.4559	1.3386	2	BRG1 form-associated factor 53A
357	1.0509	1.3033	1.5802	1.5723	1.4168	2	RIKEN cDNA 443042G14 gene
358	1.0156	1.1796	1.2639	1.2773	1.2013	2	Mus musculus, similar to CG1-147 protein, clone MGC25743 IMAGE399061, mRNA, complete cds
359	1.1919	1.6059	1.9140	1.9248	1.5416	2	human receptor 1 (GRD, ribosomal protein S4)
360	1.1772	1.3871	1.5238	1.5783	1.3957	2	UDP-N-acetyl-alpha-D-glucosamine(N-acetyl hexanaminyl)-galactose 4-epimerase/beta-1,4-N-acetylglucosaminyl transferase
361	0.9918	1.3559	1.7243	1.7036	1.4070	2	ribosomal protein L5
362	0.9236	1.3424	1.7120	1.7548	1.3982	2	ribosomal protein L5
363	1.0019	1.6503	1.6219	1.8698	1.6886	2	Unknown
364	0.9236	1.3383	1.5377	1.2969	1.6884	2	claudin 4
365	0.8999	1.1923	1.4612	1.2969	1.2125	2	E76 avian leukemia oncogene 2, 3' domain
366	1.0054	1.1923	1.4612	1.6057	1.5306	2	scudellin 1
367	0.9720	1.5172	1.5688	1.5612	1.5255	2	tyrosine 5-monooxygenase/hydrophobic 5-monooxygenase activation protein, eta polypeptide expressed sequence A156180
368	0.9920	1.3317	1.3471	1.3404	1.3515	2	tissue inhibitor of metalloproteinase
369	1.0953	3.0749	3.0193	2.8424	2.8680	2	SV40/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily 4, member 5
370	0.9175	1.1528	1.1179	1.1179	1.1417	2	member 5
371	1.0293	1.2172	1.2430	1.2245	1.2593	2	BC12-antagonist/21er 1
372	0.9142	1.7542	1.6654	1.7801	1.7848	2	auxin A5
373	1.0614	1.5743	1.5697	1.5836	1.6713	2	core promoter element binding protein
374	0.8819	1.6174	1.9000	1.7364	1.4644	2	ribosomal protein S4, X-linked
375	1.0486	2.0169	2.3995	2.1620	1.9031	2	SFB domain binding glutamate acid-rich protein-like 3
376	1.1791	1.8132	1.9319	1.9017	1.7616	2	phosphoglycerate kinase EPI_3
377	0.9477	1.2291	1.2628	1.2879	1.1819	2	ubiquitin-conjugating enzyme E2I_3
378	0.9927	1.0910	1.1130	1.0879	1.0874	2	Mus musculus, similar to hypothetical protein FLJ13213, clone MGC23855 IMAGE420628, mRNA, complete cds
379	1.0583	1.3916	1.4379	1.3821	1.3659	2	DNA segment, Chr 17, ERATO Dst 441, expressed
380	0.9285	1.8598	2.1680	1.7429	2.0043	2	transforming growth factor, beta induced, 68 kDa
381	0.9997	1.3814	1.2499	1.1804	1.2053	2	oncoprotein translation initiation factor 4, gamma 2
382	1.0108	1.7742	2.1777	2.6390	2.4383	2	lymphocyte antigen 6 complex, locus E
383	0.9871	1.1141	1.1763	1.2068	1.1977	2	RIKEN cDNA 492152B07 gene
384	0.8993	1.3005	1.3760	1.4886	1.4806	2	amaadin A6
385	1.0427	1.3580	1.4405	1.4577	1.4921	2	ribosomal protein S23
386	1.0454	1.2103	1.2506	1.2689	1.2617	2	protein tyrosine phosphatase, non-receptor type 9
387	1.0722	1.3211	1.3274	1.4337	1.4424	2	Unknown
388	0.9676	1.3432	1.3314	1.4721	1.5478	2	cellar cycle translation initiation factor 4A1

389	0.9192	1.3767	1.4751	1.5131	1.7564	2	Baculoviral IAP repeat-containing 1a
390	1.0092	1.3138	1.4509	1.4923	1.5790	2	perlecanin alpha
391	0.9321	1.1637	1.2866	1.3667	1.3767	2	CD5 related protein 21 complex, subunit 1 (21 kDa)
392	1.0014	1.2887	1.5769	1.8269	1.8593	2	CD5 antigen
393	1.0693	1.2970	1.4700	1.5469	1.5769	2	Unknown
394	0.8751	1.1307	1.4512	1.7149	1.4358	2	Mass nuclein. Similar to dendritic cell protein, clone MGC:11741 IMAGE3960335, mRNA, complete cds
395	0.8679	1.4380	1.6503	1.5282	1.5450	2	hemopoietic cell phosphatase
396	1.0612	1.2098	1.2772	1.2516	1.2652	2	2'-5' oligoadenylate synthetase 1A
397	1.0200	1.2776	1.3701	1.3446	1.3559	2	DNA segment, Chr 12, ERATO D01 604, expressed
398	1.0539	1.2715	1.3036	1.2651	1.2672	2	thymosin, beta 4, X chromosome
399	0.9107	1.7153	2.3956	2.3542	2.2252	2	small inducible cytokine B subfamily (Cys-X-Cys), member 10
400	0.9790	1.3101	1.6005	1.5099	1.5488	2	AXL receptor tyrosine kinase
401	0.9711	1.4342	1.9607	1.4200	1.8099	2	small inducible cytokine A9
402	1.0407	1.2827	1.2267	1.1205	1.1935	2	SAF1a gene homolog (S. cerevisiae)
403	1.1581	1.4242	1.7527	1.3748	1.6223	2	small inducible cytokine A7
404	1.1344	1.2385	1.3246	1.1894	1.2853	2	nestin
405	0.9768	1.1650	1.2693	1.0482	1.1947	2	Mass muscular, clone MGC:19161 IMAGE4242170, mRNA, complete cds
406	1.0085	1.1659	1.1872	1.1016	1.1799	2	granular cell type 2 O-antigenase 1
407	0.9570	1.2726	1.4005	1.0838	1.1799	2	granular cell type 2 O-antigenase 1
408	0.8979	1.1824	1.3833	1.0459	1.1947	2	granular cell type 2 O-antigenase 1
409	0.7971	1.2145	1.3833	1.0459	1.1947	2	granular cell type 2 O-antigenase 1
410	0.9159	1.2615	1.2057	1.2604	1.4408	2	granular cell type 2 O-antigenase 1
411	0.9910	1.2370	1.3846	1.3575	1.4669	2	immunoglobulin superfamily, member 8
412	0.9910	1.2370	1.3846	1.3575	1.4669	2	immunoglobulin superfamily, member 8
413	1.1674	1.3938	1.3242	1.1783	1.3402	2	cell division cycle 42 homolog (S. cerevisiae)
414	0.9558	1.3022	1.2894	1.3312	1.4198	2	RIKEN cDNA 4930506A07 gene
415	1.0976	1.2601	1.2696	1.2100	1.3906	2	diaphorase 1 (NADH)
416	0.8633	1.1617	1.2776	1.0506	1.4714	2	phorbol-12-myristate-13-acetate-induced protein 1
417	0.9780	1.1367	1.2423	1.1320	1.3682	2	phorbol-12-myristate-13-acetate-induced protein 1
418	1.0087	1.3615	1.3483	1.2931	1.3871	2	phorbol-12-myristate-13-acetate-induced protein 1
419	0.9741	1.3756	1.4229	1.3068	1.4986	2	phorbol-12-myristate-13-acetate-induced protein 1
420	0.9006	1.3014	1.4278	1.2439	1.4480	2	phorbol-12-myristate-13-acetate-induced protein 1
421	0.8681	1.3985	1.8253	1.3655	1.4480	2	phorbol-12-myristate-13-acetate-induced protein 1
422	0.9130	1.2445	1.2999	1.1371	1.3884	2	phorbol-12-myristate-13-acetate-induced protein 1
423	1.2153	1.2160	2.3878	2.1431	2.6374	2	phorbol-12-myristate-13-acetate-induced protein 1
424	1.0132	1.1831	1.2670	1.1613	1.2605	2	phorbol-12-myristate-13-acetate-induced protein 1
425	0.9345	0.8618	0.8351	0.7595	0.6684	3	phorbol-12-myristate-13-acetate-induced protein 1
426	0.8801	0.8281	0.7446	0.8023	0.6418	3	phorbol-12-myristate-13-acetate-induced protein 1
427	0.8391	0.4198	0.6520	0.6794	0.4942	3	phorbol-12-myristate-13-acetate-induced protein 1
428	0.9140	0.4199	0.3362	0.6193	0.5699	3	phorbol-12-myristate-13-acetate-induced protein 1
429	1.1527	0.5483	0.7967	0.9056	0.9320	3	phorbol-12-myristate-13-acetate-induced protein 1
430	1.0530	0.6802	0.8739	0.9264	0.9410	3	phorbol-12-myristate-13-acetate-induced protein 1
431	0.8908	0.4317	0.5903	0.6253	0.7110	3	phorbol-12-myristate-13-acetate-induced protein 1
432	1.1135	0.5403	0.6078	0.6820	0.6861	3	phorbol-12-myristate-13-acetate-induced protein 1

433	1.0378	0.6428	0.8193	0.8424	0.8880	3	estrogen related receptor, alpha
434	0.7955	0.3840	0.5353	0.5684	0.6072	3	solute carrier family 22 (organic cation transporter), member 5
435	0.9197	0.6383	0.7685	0.7898	0.8061	3	inhibin, alpha 2
436	0.8775	0.3124	0.5760	0.7141	0.5975	3	Mus musculus, similar to hypothetical protein F121634, clone MGC:19374 IMAGE:2631696, mRNA, complete cds
437	0.9205	0.5285	0.6892	0.7204	0.6726	3	oxysterol binding protein, like 1A
438	1.0303	0.5904	0.7618	0.7590	0.7512	3	oxysterol binding protein, like 1B
439	0.9257	0.5420	0.7451	0.7508	0.7498	3	peroxisomal carnitine oxidase
440	0.7442	0.3521	0.5326	0.6378	0.6378	3	peroxisomal carnitine oxidase
441	0.9685	0.3552	0.5446	0.6980	0.6839	3	cytochrome P-450 2A6
442	0.9685	0.1439	0.4028	0.4404	0.6333	3	glycerol kinase
443	1.0339	0.6248	0.7932	0.8344	0.9307	3	solute carrier family 12, member 1
444	0.7819	0.3947	0.6001	0.5682	0.6998	3	Bta protein
445	0.9535	0.4577	0.6027	0.5602	0.6998	3	hydroxysteroid dehydrogenase-1, delta-S-3-beta
446	1.0207	0.7390	0.8378	0.9178	0.9822	3	fibulin 3
447	0.9986	0.7013	0.8551	0.9231	1.0109	3	UDP-Gal-4-epi-GlcNAc 6-epi 1,3-galactosyltransferase, polypeptide 3
448	0.9836	0.6209	0.7348	0.9121	1.0071	3	telomerase protein P, plasma 1
449	1.0329	0.5009	0.7450	0.9372	1.0031	3	Mus musculus, clone IMAGE:358987, mRNA, partial cds
450	0.9919	0.7406	0.8638	0.9475	0.9708	3	EST 1
451	1.0324	0.8305	0.9156	1.0912	0.9137	3	5-azacytidine induced gene 1
452	0.9771	0.6699	0.7176	0.8389	0.7884	3	retinol dehydrogenase 2, liver
453	0.8509	0.4999	0.6856	0.8032	0.8152	3	retinol dehydrogenase 2, liver
454	0.9063	0.7210	0.7336	0.8152	0.8102	3	neural protein with factor binding protein 4
455	1.0178	0.8135	0.9312	0.9316	0.7359	3	neural protein with factor binding protein 4
456	0.9798	0.7827	0.8312	0.9316	0.7359	3	EST A1181838
457	1.0324	0.8135	0.9312	0.9316	0.7359	3	neural protein with factor binding protein 4
458	1.1253	0.5364	0.6409	0.5984	0.8107	3	nuclear receptor coactivator 4
459	1.0182	0.8019	0.8445	0.9453	0.8437	3	RIKEN cDNA 110002C08 gene
460	1.0078	0.5956	0.6854	0.8644	0.7061	3	RIKEN cDNA 120001D11 gene
461	1.0362	0.8239	0.8753	0.9706	0.8768	3	expressed sequence A480660
462	0.9929	0.3315	0.6021	0.7369	0.6669	3	heat-responsive protein 12
463	1.0401	0.7373	0.8051	0.9084	0.8444	3	lactate dehydrogenase A, ligase, GDP-forming, beta subunit
464	0.8619	0.5529	0.6597	0.7155	0.6589	3	glutathione transferase zeta 1 (maleylacetate-ethyl transferase)
465	0.8571	0.4509	0.7141	0.6130	0.5382	3	RIKEN cDNA 061001114 gene
466	1.1680	0.7192	0.8663	0.9687	0.8814	3	cytochrome c oxidase subunit 1b, Pst 3
467	0.9757	0.7262	0.7046	0.8461	0.7637	3	expressed sequence A4835705
468	1.0104	0.3872	0.7190	0.8710	0.7150	3	RIKEN cDNA 131001380 gene
469	1.1357	0.5359	0.6727	0.9716	0.8641	3	phosphotyrosine Cdk2-antagonist (emopamil) binding protein
470	1.0571	0.6239	0.7190	0.9716	0.8641	3	phosphotyrosine Cdk2-antagonist (emopamil) binding protein
471	0.9352	0.5198	0.6198	0.7046	0.6583	3	FK506 binding protein 12-epitope associated protein 1
472	1.0352	0.5198	0.6198	0.7046	0.6583	3	RIKEN cDNA 0610006N12 gene
473	1.1953	0.7803	0.8830	0.8894	0.9492	3	RIKEN cDNA 181005A013 gene
474	1.0970	0.6433	0.7445	1.0358	0.8419	3	RIKEN cDNA 2310051E17 gene
475	0.8446	0.5412	0.6005	0.8320	0.6665	3	mitogen activated protein kinase 13
476	1.1011	1.3217	1.3461	1.1891	1.0091	4	DNA primase, p49 subunit
477	1.1221	1.3644	1.4586	1.2110	1.0056	4	DNA primase, p49 subunit

478	1.0254	1.2717	1.3756	1.1513	0.9416	4	chitinase 3-like 3
479	1.1328	1.4784	1.7963	1.4788	0.9639	4	ribosomal protein L28
480	1.1227	1.3355	1.4238	1.2682	0.9761	4	Mus musculus, similar to hypothetical protein MG3133, clone MGC:1396 IMAGE3465951, mRNA, complete cds
481	1.0459	1.1818	1.2658	1.1469	0.9606	4	ubiquitin-like 1 (centrin) activating enzyme H1A
482	1.0693	1.1402	1.2053	1.1283	1.0173	4	expressed sequence A495377 IMAGE3499365, mRNA, complete cds
483	1.0628	1.1156	1.2016	1.1337	0.9083	4	Mus musculus, clone MGC:5377 IMAGE3499365, mRNA, complete cds
484	1.0628	1.1820	1.2455	1.1398	0.9300	4	RIKEN cDNA, 1610511O17 gene
485	1.0948	1.2156	1.2584	1.1247	0.9444	4	RIKEN cDNA, 1100101L19 gene
486	0.9522	1.2425	1.1062	1.0803	0.8774	4	nitric acid induced 1
487	1.0865	1.4441	1.2235	1.1786	0.9942	4	RIKEN cDNA, 1810023B24 gene
488	0.9952	1.2036	1.1622	1.1417	0.9449	4	transposon-derived growth factor
489	1.0214	1.1893	1.1494	1.1261	0.9839	4	steroid receptor RNA activator 1
490	0.9646	1.1555	1.1351	1.0752	0.9945	4	schlafen 4
491	1.2059	1.2836	1.5301	1.3439	1.0903	4	lactate dehydrogenase 1, A chain
492	1.1800	1.2588	1.4462	1.3466	1.1501	4	Mus musculus, clone IMAGE:4455744, mRNA, partial cds
493	1.1552	1.2438	1.4716	1.2866	1.1167	4	regulator of G-protein signaling 19 interacting protein 1
494	1.0002	1.0878	1.2716	1.2027	0.8901	4	granovine diphosphate (GDP) dissociation inhibitor 3
495	0.9514	1.1888	1.4098	1.5523	0.9862	4	dehydro-diphosphoglycerate-protein glyoxyltransferase
496	0.9355	1.1888	1.4317	1.4925	1.0033	4	procollagen, type I, alpha 1
497	1.1346	1.4761	1.6092	1.5930	1.1651	4	ribosomal protein L8
498	0.9700	1.1317	1.2124	1.1458	1.0059	4	perlecan/prolyl 4-hydroxylase (cyclophilin)-like 1
499	0.9720	1.6647	2.0127	1.6587	1.1292	4	acidic ribosomal phosphoprotein PO
500	1.1094	1.7959	2.0748	1.7960	1.1524	4	ribosomal protein S2
501	1.0387	1.8326	2.1030	2.1386	1.1389	4	ribosomal protein L10A
502	0.9881	1.6212	1.9203	1.8679	1.2607	4	ribosomal protein L19
503	1.0133	1.7517	2.4000	2.5281	1.3440	4	RIKEN cDNA, 1810009A01 gene
504	1.0884	1.8947	2.2731	2.2752	1.3118	4	ribosomal protein, large, P1
505	1.0083	1.1448	1.2145	1.2256	1.0605	4	ribosomal protein, small, P1
506	1.1156	1.8020	2.2258	1.7422	1.3432	4	expressed sequence C36302
507	1.0772	1.5091	1.6712	1.4961	1.2653	4	Mus musculus, basic transcription factor 3, clone MGC:6799 IMAGE2648048, mRNA, complete cds
508	1.0513	1.7752	2.2322	1.9914	1.2727	4	cathepsin D
509	1.0558	1.7174	2.0719	1.9098	1.3513	4	ribosomal protein S7
510	1.0519	1.4563	1.7487	1.6553	1.2705	4	RIKEN cDNA, 061002G013 gene
511	1.0310	1.6740	2.0161	1.7487	1.3056	4	topomycin A-like S15
512	0.9851	1.4157	1.6599	1.5067	1.2141	4	RIKEN cDNA, 301001A07 gene
513	0.9221	1.4267	0.7881	1.1023	1.2316	5	AB binding protein 1
514	0.9981	0.9938	0.8378	1.3772	1.4072	5	nuclear receptor subfamily 2, group F, member 2
515	1.0544	1.0451	0.9600	1.2568	1.3653	5	nuclear protein GU2
516	1.0441	1.0086	0.9497	1.2215	1.3852	5	RIKEN cDNA, 1700016A15 gene
517	1.0677	1.0196	1.0156	1.2401	1.2842	5	protein, lysine phosphatase, receptor type, C, polypeptide-associated protein
518	1.1450	1.0074	1.0750	1.0170	1.6983	5	expressed sequence C80611
519	1.0490	0.9791	1.0259	1.3343	1.3794	5	expressed sequence C83517
520	1.1572	1.0877	1.0899	1.3343	1.2886	5	protein, lysine phosphatase, receptor type, O
521	1.0744	1.0001	1.0402	1.2953	1.2529	5	

522	1.0688	0.9723	1.0203	1.3206	1.2484	5	bone morphogenetic protein receptor, type 1A
523	1.1004	0.9990	1.0658	1.2307	1.2252	5	RIKEN cDNA 2610302D2 gene
524	0.9396	0.7401	0.7912	0.9353	0.9894	5	transcription factor 2 domain-containing transforming protein D
525	0.9598	0.9998	1.0042	1.3665	0.9744	5	transcription factor 4
526	0.6687	0.8222	0.7939	0.9744	0.9744	5	ESTs
527	0.7666	0.8264	0.8021	1.1708	1.1708	5	peptidyl/lysyl isomerase C
528	1.1335	0.9919	1.3151	1.4512	1.4512	5	RIKEN cDNA 311002IN18 gene
529	0.8920	0.7734	0.7748	1.0905	1.1534	5	specie-type POZ protein
530	1.0497	0.9375	0.9611	1.2325	1.2627	5	ESTs, Weakly similar to simple repeat sequence-containing transcript (Mus musculus) (M.musculus)
531	1.1195	0.8571	1.2821	1.6795	1.8423	5	transcription factor 21
532	1.1442	0.9930	1.3094	1.6671	1.7597	5	macrophage scavenger receptor 2
533	1.1838	1.0801	1.2406	1.2964	1.4212	5	ras homolog D (RhoD)
534	0.9662	0.9097	1.1485	1.2346	1.4239	5	ESTs
535	1.2090	1.1308	1.3565	1.4311	1.5207	5	cell-like receptor 2
536	0.9932	0.8051	0.8644	1.6714	2.4657	5	RIKEN cDNA 110032A13 gene
537	0.9638	0.8947	0.9198	1.1563	1.2490	5	expressed sequence tag 848469
538	0.9534	0.8621	0.9194	1.1748	1.3264	5	expressed sequence tag 848469
539	1.0082	0.9228	0.9540	1.1534	1.3264	5	DNA segment, Chr 8, Brigham & Women's Genetics 1112 expressed
540	1.0235	0.9920	0.9787	1.1733	1.3264	5	serifin-dependent neuroprotective protein
541	1.1077	1.0387	1.0953	1.1733	2.3854	5	matrix metalloproteinase 7
542	1.1479	0.9773	1.0953	1.2190	2.5423	5	expressed sequence A194696
543	0.9860	0.8716	0.9622	1.4171	2.0503	5	retinoic acid early transcript gamma
544	1.0367	0.9216	0.9622	1.4171	2.0503	5	complement factor H related protein 3M/5G4
545	0.9563	0.9374	1.1443	1.3669	1.6479	5	early development regulator 2 (homolog of polyomeric 2)
546	0.8903	0.8374	1.0664	1.1918	1.3697	5	gamma-glutamyl hydrolase
547	0.8903	0.7658	1.0432	1.4121	1.8760	5	decortin
548	1.0382	0.9776	1.0743	1.1949	1.3736	5	myocyte enhancer factor 2A
549	1.0094	0.9922	1.0062	1.3025	1.5197	5	histocompatibility 2, class II antigen A, alpha
550	0.9496	0.7367	1.0097	2.1319	2.8834	5	complement component factor H related protein 3
551	1.1506	0.8278	1.2538	2.4083	3.8563	5	histocompatibility 2, class II antigen A, alpha
552	1.0345	0.9905	1.0673	1.2326	1.3108	5	ganglioside-induced differentiation-associated-protein 3
553	1.0058	0.9940	1.2666	1.3443	1.8569	5	ganglioside-induced differentiation-associated-protein 3
554	1.0538	0.9892	1.1895	1.1994	1.5792	5	ESTs, Weakly similar to 202311A4, granule cell marker protein (M.musculus)
555	0.9533	1.0053	1.1020	1.2514	1.5792	5	ESTs, Weakly similar to 202311A4, granule cell marker protein (M.musculus)
556	1.0788	1.0856	1.1943	1.2514	1.5792	5	RIKEN cDNA 231004G015 gene
557	1.0682	1.0637	1.1359	1.2524	1.3753	5	RIKEN cDNA E130113K08 gene
558	1.0759	1.1409	1.2024	1.6449	2.1164	5	interferin-associated protein
559	0.9353	1.1409	1.2024	1.6449	2.1164	5	CD48 antigen
560	0.8822	1.1251	1.4436	1.4436	1.8141	5	serine protease inhibitor 6
561	0.9490	0.9775	1.1514	1.7313	1.3618	5	ubiquitin-conjugating enzyme E2D 2
562	0.9889	0.8678	1.3518	1.8748	1.8466	5	RAS-related Gs totalitum substrate 2
563	1.0452	1.0441	1.1399	1.2733	1.1817	5	glypican 3
564	1.0777	1.0690	1.1755	1.3873	1.2101	5	Mus musculus, Similar to hypothetical protein FI2045, clone MGC7940 IMAGE5384061, expressed sequence A042434
565	1.0284	1.0269	1.2169	1.6528	1.3402	5	expressed sequence A042434
566	1.0284	1.0269	1.2169	1.6528	1.3402	5	benzodiazepine receptor, postnatal

566	1.1138	1.1173	1.1857	1.3590	1.2334	5	RIKEN cDNA 332140 cDNA gene
567	1.0393	0.9358	1.0422	1.3203	1.1945	5	hemochromatosis
568	1.2057	1.1632	1.2238	1.3369	1.2510	5	RIKEN cDNA 181045007 gene
569	1.0767	0.9953	1.1008	1.4273	1.2152	5	expressed sequence A051333
570	0.7786	0.8853	1.2764	1.6380	1.8390	5	chromosome 10
571	0.8371	0.8313	1.1095	1.3446	1.3115	5	calcium channel, voltage-dependent, beta 3 subunit
572	1.0900	1.2170	1.7844	1.3158	1.3188	5	neurofibrosarcoma expressed gene 1
573	0.8738	0.9131	1.1708	1.2927	2.2251	5	T-cell specific GTPase
574	0.8187	0.9131	1.1708	1.2927	2.2251	5	centrin 3
575	0.8187	0.9131	1.1708	1.2927	2.2251	5	lysosomal-associated protein transmembrane 5
576	0.9398	1.1495	1.3851	2.1191	2.0841	5	chloride channel calcium activated 1
577	1.0142	1.2999	2.1261	4.4031	4.3267	5	cathepsin S
578	0.9640	1.0862	1.2569	1.8391	1.5971	5	protein tyrosine phosphatase, receptor type, C
579	1.0523	1.1920	1.2192	1.3611	1.5243	5	expressed sequence A1604920
580	0.8848	1.1392	1.1614	1.3111	1.4113	5	nucleotide related transcription factor 1
581	0.9640	1.2690	1.3659	1.9377	2.2444	5	oncosterin receptor
582	0.9036	1.0784	1.0787	1.3259	1.4879	5	neuropilin
583	0.9313	1.1539	1.3170	2.1477	3.3642	5	CD52 antigen
584	1.0126	1.1442	1.2098	1.6038	2.0581	5	histocompatibility 2, class II, beta DNA
585	0.9198	0.9953	1.1206	1.3312	1.5158	5	ESTs, Moderately repetitive, to T46312 hypothetical protein DKFZp4541111.1 (H-asptase)
586	0.9171	1.0215	1.0601	1.3413	1.4274	5	transmembrane repeat domain
587	0.9802	1.0350	1.2201	1.5846	1.4274	5	protein S (alpha)
588	0.9717	1.0447	1.0716	1.2566	1.3751	5	Mus musculus, clone MGC:312159 BMAGE3171109, mRNA, complete cds
589	0.9336	1.0193	1.2116	1.2755	1.2960	5	expressed sequence A413331
590	0.9336	1.0193	1.2116	1.2755	1.2960	5	myristoylated alanine rich protein kinase C substrate
591	0.9650	0.9591	1.3077	1.9038	1.7718	5	RIKEN cDNA 2410026K10 gene
592	1.0140	1.0864	1.2061	2.0306	1.8587	5	microfibrillar associated protein 5
593	1.0032	0.9118	1.1683	1.4592	1.4295	5	matrix metalloproteinase 2
594	1.0696	1.0149	1.1799	1.4794	1.4837	5	RIKEN cDNA 2810418P01 gene
595	1.0701	0.9878	1.3489	1.8957	1.8346	5	Mus musculus, Similar to DKFZp366b0621 protein, clone MGC:31865 BMAGE3535789, mRNA, complete cds
596	1.1047	0.8042	1.7386	4.4517	4.2955	5	he-associated invariant chain
597	0.8360	0.9664	1.0969	1.6065	1.4526	5	hydrogen 1
598	0.7294	0.9189	1.1719	2.2828	1.8126	5	matrix metalloproteinase 14 (membrane-located)
599	1.0682	1.1253	1.2076	1.4741	1.5733	5	RIKEN cDNA 261020N023 gene
600	0.9714	1.1162	1.4890	2.6282	2.1812	5	expressed sequence A113321
601	1.0294	1.1744	1.4273	2.6282	1.8306	5	hemopoietic specific 1
602	1.0111	1.0553	1.1917	2.1917	5.5060	5	matrix gamma-carboxyglutamate (Gla) protein
603	0.8601	0.9601	1.3026	1.7400	1.2764	5	Fox apoptotic inhibitory molecule
604	1.0774	1.2432	1.3929	3.1921	3.0027	5	antibiotic binding protein 1 (amine oxidase, copper-containing)
605	0.9645	0.8830	0.9929	1.3430	2.8276	5	RIKEN cDNA 3021401A05 gene
606	1.1142	1.0943	1.1180	1.2988	1.2559	5	laminin, alpha 2
607	1.1579	0.9502	1.2503	1.7561	1.7967	5	RIKEN cDNA 231002K15 gene
608	1.0163	0.9402	1.0338	1.2297	1.2130	5	cyrtatin C
609	1.0341	0.9362	1.0558	1.2459	1.2236	5	expressed sequence A1843940
610	1.0341	0.9362	1.0558	1.2459	1.2236	5	hafloranferase-related protein SUT-1X1



611	1.1487	1.1234	1.3384	1.9175	2.3082	5	EGF-like module containing, mucin-like, hormone receptor-like sequence 1
612	1.0326	1.0690	1.1895	1.5144	1.7217	5	apolipoprotein B capping complex 1
613	1.1007	1.1309	1.5867	2.9748	3.5907	5	vascular cell adhesion protein 1
614	1.1983	1.1120	1.3545	1.9983	2.1804	5	cytosect sequence A774384
615	1.0716	1.0252	1.2573	1.8115	1.8775	5	serpinone (proteinase inhibitor, beta type 8 large multifunctional protease 7)
616	1.0003	0.9941	1.0611	1.5084	1.6069	5	serpinone (proteinase inhibitor, beta type 8 large multifunctional protease 7)
617	1.0292	1.0219	1.0399	1.248	1.4029	5	ESR1s
618	1.0050	1.0411	1.1613	1.451	1.7845	5	chemokine orphan receptor 1
619	1.1305	0.9488	1.1613	2.4045	2.4045	5	serine (or cysteine) proteinase inhibitor, clade G (C1 inhibitor), member 1
620	1.1012	0.9488	1.1613	2.4045	2.4045	5	Unknown
621	1.0312	0.9979	1.0620	1.3125	1.2872	5	ESR1s
622	0.9379	1.0466	1.1406	1.8888	1.9354	5	RIKEN cDNA 270033M7 gene
623	1.0088	1.0616	1.1703	1.7674	1.8580	5	serine (or cysteine) proteinase inhibitor, clade E (peptin, plasminogen activator inhibitor type 1), member 2
624	1.0431	1.1275	1.3204	2.1770	2.0270	5	Mus musculus, Similar to unc93 (C-degans) homolog B, clone MGC3567 IMAGE4039296, member 2
625	0.9776	0.9898	1.0467	1.2738	1.2766	5	mRNA, complete cds
626	0.9918	1.0013	1.1452	1.6077	1.5515	5	Cyidine 5-triphosphate synthase 2
627	0.7574	0.8055	1.0105	1.7275	1.6969	5	beta-mannosidase MGC51833 IMAGE344986, mRNA, complete cds
628	0.9722	1.2339	1.0575	1.7831	1.5715	5	apolipoprotein E
629	1.0529	1.2319	1.1334	1.4740	1.3073	5	apolipoprotein family 34 (sodium phosphate), member 2
630	0.9213	1.0310	0.9566	1.3671	1.2054	5	NCX-associated protein 1
631	1.0406	1.3406	1.0936	1.7840	1.5690	5	max binding protein
632	1.1209	1.1850	1.3529	1.5690	1.4581	5	platelet-derived growth factor, B polypeptide
633	0.9676	1.1340	1.0837	1.4115	1.3635	5	expressed sequence AA408783
634	1.0822	1.1773	1.1551	1.3483	1.3255	5	Mus musculus, Similar to nuclear cysteine-rich protein, clone MGC6718 IMAGE336161, mRNA, complete cds
635	0.9486	1.0770	1.0557	1.3062	1.3189	5	iron-catalytic region of tyrosine kinase adaptor protein 1
636	1.0654	1.1699	1.1703	1.3650	1.3592	5	ring finger protein (C3HC4 type) 19
637	1.0663	1.1543	1.1307	1.5507	1.5017	5	specitin SH3 domain binding protein 1
638	0.9880	1.0673	1.0618	1.3613	1.2816	5	Unknown
639	0.9882	1.1152	1.1118	1.4444	1.3711	5	protein kinase C delta
640	0.8215	0.9317	1.0560	1.6204	1.5544	5	protein factor of kappa light chain gene enhancer in B-cells 1, p105
641	0.7657	0.9373	0.9616	1.3524	1.2884	5	ESR1s
642	0.9198	1.0226	0.9517	1.2594	1.3166	5	X (tactivo)-specific transcript, antisense
643	0.9518	1.0226	0.9517	1.2594	1.3166	5	RIKEN cDNA 493242K08 gene
644	0.9442	0.9759	0.9992	1.2405	1.2420	5	platelet-activating factor acetylhydrolase, isoform 1b, alpha subunit
645	0.9084	0.9759	0.9992	1.2405	1.2420	5	mannose-6-phosphate receptor, cation dependent
646	1.0076	1.0124	1.0124	1.2777	1.3606	5	RIKEN cDNA 563040J11 gene
647	1.1655	1.1799	1.1442	1.6088	1.4724	5	RIKEN cDNA 1110007F23 gene
648	0.9389	0.9627	0.9283	1.3902	1.2895	5	LIM and SH3 protein 1
649	0.9970	1.1310	1.0875	1.3903	1.2864	5	casein kinase 1, epsilon
650	1.0015	1.1491	1.1002	1.4888	1.3856	5	alt homolog 3 (Drosophila)
651	0.9043	0.9824	0.9356	1.3423	1.2115	5	myeloid differentiation primary response gene 88
652	0.9322	0.9731	0.9709	1.3387	1.3894	5	90c-2 (suppressor of clear) homolog (C. elegans)
653	0.9735	1.0119	1.0127	1.3834	1.3779	5	expressed sequence A447431
						5	small inducible cytokine B subfamily, member 5

654	1.1007	1.1386	1.0671	1.7571	1.7613	5	Mus musculus, Similar to hypothetical protein FLJ20234, clone MGC37525 IMAGE:596113, mRNA, complete cds
655	0.9826	0.9894	0.9796	1.1840	1.2036	5	expressed sequence C80013
656	1.0175	1.1162	1.0893	1.3116	1.3979	5	RIKEN cDNA 111009B24 gene
657	1.0337	1.1857	1.1143	1.7017	1.8476	5	growth differentiation factor 3
658	1.0176	1.1136	1.0950	1.3396	1.4888	5	growth differentiation factor 3
659	0.9736	0.9596	0.9385	1.3152	1.4888	5	muscle-specific protein containing 11 (TIR-associated protein, 230 kDa subunit)
660	1.1651	1.3062	1.2279	2.4757	2.4757	5	Mus musculus, clone IMAGE:4952483, mRNA, partial cds
661	0.9625	1.0744	1.0744	1.3779	1.6105	5	basalophilic LAP repeat-containing 3
662	0.9360	1.0291	1.0291	1.2046	1.2408	5	expressed sequence AW493404
663	0.9360	1.0291	1.0291	1.2046	1.2408	5	Unknown
664	0.9137	1.0501	1.0220	1.2927	1.3836	5	y-tail domain leukemia viral oncogene homolog A (ms related)
665	1.0262	1.1734	1.1469	1.3032	1.3956	5	RIKEN cDNA 913001J04 gene
666	1.0714	1.3009	1.2839	1.4240	1.5933	5	CD72 mitogen
667	1.0738	1.2333	1.2035	1.3765	1.7536	5	expressed sequence AB14027
668	1.0207	1.1500	1.2085	1.2554	1.5021	5	S100 calcium binding protein A13
669	0.9480	1.0927	1.1333	1.1594	1.3868	5	glycoprotein 49 A
670	1.0865	1.4790	2.1189	1.5922	2.3346	5	TYRO protein tyrosine kinase binding protein
671	1.1369	1.4819	2.3374	1.8822	2.4631	5	anion-binding protein 4
672	1.1111	1.1784	1.4835	1.2924	1.4067	5	anion-binding protein 4
673	1.0404	1.0488	1.4157	1.2505	1.4067	5	anion-binding protein 4
674	1.1808	1.2468	1.1460	1.2342	1.4067	5	anion-binding protein 4
675	0.9743	0.9563	1.3571	1.2505	1.4067	5	anion-binding protein 4
676	0.9849	0.9986	1.3571	1.2505	1.4067	5	anion-binding protein 4
677	1.0156	0.9986	1.3571	1.2505	1.4067	5	anion-binding protein 4
678	1.0156	0.9986	1.3571	1.2505	1.4067	5	anion-binding protein 4
679	1.0254	0.9752	1.2561	1.8031	1.6175	5	RIKEN cDNA 120013A08 gene
680	1.0739	0.9786	1.2602	1.4657	1.8654	5	beta-2 microglobulin
681	1.1453	1.1106	1.3561	1.4374	1.3412	5	guanylate nucleotide binding protein 2
682	1.0831	1.1017	1.3415	1.4836	1.3384	5	expressed sequence AW47381
683	1.0102	1.0105	1.2104	1.2955	1.3482	5	expressed sequence A4448003
684	0.9604	1.1147	1.1871	1.2848	1.2713	5	expressed sequence A4448003
685	0.8352	1.1384	1.4695	1.7288	1.4119	5	Yamaquela sarcoma viral (v-vy) oncogene homolog
686	1.1090	1.2709	1.3923	1.4400	1.3966	5	RIKEN cDNA 120009B18 gene
687	1.0209	1.1713	1.4081	1.4364	1.3966	5	B-cell leukemia/lymphoma 2 related protein A1b
688	1.1939	1.2568	1.3188	1.3272	1.4035	5	RIKEN cDNA 119006C12 gene
689	0.9783	1.0780	1.6032	2.4458	2.4035	5	expressed sequence A007865
690	1.0895	1.2245	1.3802	2.4458	2.4035	5	proteasome activator 1
691	1.0256	1.1604	1.3802	2.4458	2.4035	5	proteasome activator 1
692	0.9593	1.0544	1.6343	1.4977	2.9947	5	CD123 antigen
693	0.9861	1.1918	1.5151	1.8749	1.4916	5	Unknown
694	1.0252	1.2281	1.4217	1.6569	1.6888	5	proteasome (prosome, macropain) 28 subunit, alpha
695	1.0252	1.2281	1.4217	1.6569	1.6888	5	calponin 2
696	1.1009	1.2982	2.1060	2.0360	1.6374	5	aldolase-dehydrogenase family 1, subfamily A2
697	1.0192	1.1598	1.3064	1.3476	1.4013	5	Pe receptor, Igf, high affinity 1, gamma polypeptide
698	0.9578	2.0401	3.9311	5.1872	6.5144	5	expressed sequence A1504062
						5	lysosyme

699	0.9370	1.3643	1.8445	1.9401	2.2436	5	internal killer kinase recognition sequence
700	1.1083	1.2251	1.3340	1.3925	1.5340	5	Box and SPRY domain containing
701	0.9443	1.2390	1.6405	1.6112	1.7033	5	RIKEN cDNA 2700381K18 gene
702	0.9918	1.1699	1.4842	1.4897	1.6132	6	RIKEN cDNA 1700019E19 gene
703	1.0606	1.2121	1.2335	1.2176	1.2906	6	surfeit gene 4
704	1.1066	1.1989	1.2375	1.3779	1.1873	6	RIKEN cDNA 2310073M15 gene
705	0.9315	1.1838	1.2647	1.5802	1.4909	6	guanine nucleotide binding protein, alpha inhibiting 2
706	0.9344	1.4701	1.5832	1.3265	1.2855	6	capping protein beta 1
707	0.9549	1.2048	1.3368	1.3922	1.3869	6	coronin, actin binding protein 1B
708	1.0959	1.2048	1.3368	1.3922	1.2038	6	amclogenin
709	1.0390	1.1563	1.3441	1.6285	1.2848	6	endoplasmic reticulum protein 29
710	1.0421	1.2188	1.3668	1.3628	1.3618	6	dyadastem of tyrosine kinase 1
711	1.0830	1.1883	1.2031	1.3176	1.1567	6	RAB11a, member RAS oncogene family
712	1.0836	1.1567	1.1889	1.3176	1.1567	6	opioid growth factor receptor
713	1.0122	1.2117	1.1438	1.5175	1.1604	6	beta-glucuronidase structural
714	1.0122	1.1928	1.2095	1.5860	1.0730	6	RS13
715	1.1492	1.1032	1.3034	1.4873	1.2344	6	guanine nucleotide binding protein (G protein), gamma 2 subunit
716	1.1432	1.1704	1.3000	1.4547	1.2248	6	expressed sequence AU019833
717	1.0719	1.0800	1.2977	1.4416	1.2855	6	plasma membrane protein
718	1.0633	1.0952	1.3470	1.4600	1.2985	6	plasma membrane protein
719	1.0323	1.1273	1.2632	1.3600	1.3463	6	plasma membrane protein
720	1.0174	1.1122	1.2632	1.3600	1.3463	6	plasma membrane protein
721	1.0978	1.1172	1.4770	1.3142	1.1985	6	plasma membrane protein
722	1.1797	1.1379	1.4399	1.5275	1.2700	6	melanoma antigen, family D 2
723	1.1797	1.2266	1.3528	1.4180	1.2318	6	diacylglycerol-induced-like 3
724	0.9184	1.0715	1.4088	1.4801	1.1810	6	selectin, platelet (P-selectin) ligand
725	0.9381	1.0954	1.2662	1.3941	1.1584	6	a disintegrin-like and metalloprotease (copolysin type) with fibronectin type 1 motif 2
726	1.0433	1.2005	1.4448	1.6054	1.3142	6	myosin light chain, alkali, nonmuscle
727	1.0452	1.2868	1.7335	1.8206	1.2690	6	complement component factor 1
728	1.1323	1.3474	1.5375	1.6888	1.2981	6	small nuclear ribonucleoprotein D0
729	0.7812	1.1898	0.9419	1.2555	1.3221	6	vesicular-associated protein transmembrane 4A
730	0.8744	1.1469	0.9262	1.2769	1.2876	6	split hand foot defect gene 1
731	0.9975	1.1717	1.1286	1.7019	1.7656	6	unconjugated alpha 1
732	1.0677	1.3859	1.6233	1.8310	1.7656	6	unconjugated alpha 1
733	1.0888	1.4078	1.7599	2.1624	1.8039	6	unconjugated alpha 1
734	0.9344	1.4578	2.1769	2.2035	2.2035	6	unconjugated alpha 1
735	0.7933	1.1273	1.6061	2.1567	1.6828	6	unconjugated alpha 1
736	0.9314	1.1525	1.4079	1.7428	1.4970	6	unconjugated alpha 1
737	0.9886	1.2041	1.2652	1.5067	1.2539	6	unconjugated alpha 1
738	0.9618	1.3252	1.3643	1.7055	1.3774	6	unconjugated alpha 1
739	1.0742	1.2512	1.2828	1.4884	1.2954	6	unconjugated alpha 1
740	1.1303	1.3852	1.4497	1.6362	1.4616	6	unconjugated alpha 1
741	0.9848	1.3195	1.5136	1.8157	1.5076	6	unconjugated alpha 1
742	1.0394	1.2427	1.4044	1.4843	1.3419	6	unconjugated alpha 1
743	0.9672	1.3678	1.7620	1.9661	1.6435	6	unconjugated alpha 1

744	0.9743	1.2304	1.3690	1.5300	1.2976	6	RIKEN cDNA 4920533K18 gene
745	1.0390	1.2692	1.4427	1.5637	1.3237	6	cadherin 3
746	1.0108	1.4643	1.3598	1.6526	1.4907	6	small inducible cytokine subfamily D, 1
747	0.8722	1.9700	1.6928	2.3710	2.0115	6	tubulin alpha 1
748	0.8427	1.6802	1.3511	1.5522	1.8185	6	C12orf4 antigen
749	0.6657	1.5325	1.3538	1.6159	1.7194	6	growth arrest and DNA damage-inducible 45 alpha
750	0.6026	1.7575	1.3537	1.8397	1.8508	6	DNA-dependent early response, cytoprotein 1
751	1.0145	1.8748	1.6219	2.0834	2.2657	6	aurin A4
752	0.7616	1.4564	1.3144	1.4721	1.4721	6	histone deacetylase 1
753	1.0380	1.4402	1.4149	1.4871	1.3785	6	histocompatibility 2, L region
754	0.8656	1.4400	1.4739	2.0339	1.9503	6	RAB3D, member RAS oncogene family
755	0.8950	1.8132	1.4750	2.9820	2.5468	6	elongation of very long chain fatty acids (FEN1/Elo2, SUB4/Elo3, yeast)-like 1
756	0.6693	1.2338	1.2420	1.4219	1.3954	6	sakayotic translocation initiation factor 1A
757	1.0173	1.4567	1.3343	1.7486	1.3131	6	avian retroviral oncoflox viral (v-re) oncogene related B
758	1.0173	1.4567	1.3343	1.7486	1.3131	6	TG interacting factor
759	1.0173	1.4567	1.3343	1.7486	1.3131	6	ribosomal protein L12
760	0.9655	1.7159	1.6381	2.3284	1.8443	6	interferon gamma receptor
761	0.8361	1.1938	1.2435	1.5812	1.5104	6	keratin complex 1, acidic, gene 19
762	0.9506	1.3459	1.3198	1.6113	1.5104	6	procollagen, type XVIII, alpha 1
763	0.9192	1.7645	1.6582	2.5436	2.0641	6	complement component 3
764	0.7093	2.1074	2.0978	4.0372	2.9033	6	expressed sequence AV1111861
765	1.0125	1.3344	1.1188	1.6011	1.3963	6	hemolymph growth factor-binding 2
766	1.0552	1.3809	1.2440	1.5831	1.3818	6	hemolymph growth factor-binding 2
767	1.0179	1.2355	1.1883	1.5556	1.3818	6	hemolymph growth factor-binding 2
768	0.8693	1.2114	1.1883	1.5556	1.4841	6	hemolymph growth factor-binding 2
769	0.8693	1.2114	1.1883	1.5556	1.4841	6	hemolymph growth factor-binding 2
770	1.0344	2.1179	1.1759	3.3759	1.2320	6	RIKEN cDNA 2310430J06 gene
771	1.0616	1.6194	1.4664	2.0049	1.5683	6	polgi reassembly stacking protein 2
772	1.0373	1.1553	1.1530	1.3571	1.2929	6	actin, alpha 1, skeletal muscle
773	0.8842	1.1615	1.1325	1.7664	1.5932	6	histocompatibility 2, O region locus 7
774	0.8593	1.6164	1.5516	3.2577	2.6599	6	crystallin, mu
775	0.9906	1.1392	1.1858	1.4323	1.3385	6	leucocyte specific transcript 1
776	1.1755	1.2462	1.2241	1.3630	1.3044	6	TATA box binding protein-like protein
777	0.8480	1.3082	1.1658	2.0306	1.6109	6	MARCKS-like protein
778	0.8768	1.1194	1.2796	1.4636	1.2684	6	metastasis associated 1-like 1
779	0.9204	1.3418	1.2796	1.8044	1.5240	6	connective tissue growth factor
780	1.0785	1.3460	1.3040	1.6682	1.4445	6	ts rs
781	0.9374	1.3245	1.3484	1.9955	1.5619	6	visceral/ocular simulated phosphoprotein
782	0.9010	1.2372	1.2595	1.8395	1.4802	6	peridiploxy leucocyte C-associated protein
783	0.9598	1.6511	1.6283	2.7415	2.4802	6	visceral/ocular simulated phosphoprotein
784	0.9528	1.6511	1.6283	2.7415	2.4802	6	visceral/ocular simulated phosphoprotein
785	0.9852	1.6511	1.6283	2.7415	2.4802	6	visceral/ocular simulated phosphoprotein
786	0.9852	1.6511	1.6283	2.7415	2.4802	6	visceral/ocular simulated phosphoprotein
787	1.1867	1.2431	1.2465	1.4343	1.3120	6	RIKEN cDNA 513340A03 gene
788	0.9294	1.0982	1.1319	1.7482	1.4342	6	liver-specific bHLH-Zfp transcription factor
789	1.0208	0.8748	0.8032	1.1788	0.9069	7	carboxypeptidase E
							defect 1 homolog (Drosophila)

790	0.9132	0.7841	0.6910	0.9892	0.8373	7	cryptochrome 2 (photolyase-like)
791	0.9336	0.9162	0.7819	1.3519	0.9635	7	adenylate cyclase 4
792	1.2234	1.2195	1.0781	1.2454	1.2406	7	DnaI (Hsp40) homologue, subfamily C, member 5
793	0.8900	0.8102	0.8407	1.1757	1.0238	7	polybrytic kidney disease 1 homologue
794	0.9359	0.8551	0.8407	1.2236	0.9813	7	expressed sequence AW48255
795	1.1036	1.1438	0.9035	1.3485	1.1866	7	Ngl-A binding protein 2
796	1.0624	1.1438	0.9035	1.3485	1.1949	7	Mus musculus, clone NGC-3654 BMAGE-4954874, mRNA, complete cds
797	1.0624	1.0711	0.9476	1.4387	1.1986	7	transformed mouse 313 cell double minute 2
798	1.0624	1.0711	0.9476	1.4387	1.1986	7	small inducible cyclase
799	1.0624	1.0711	0.9476	1.4387	1.1986	7	Mus musculus, clone BMAGE-2491421, mRNA, partial cds
800	1.0184	1.0863	0.9967	1.3505	1.2389	7	Unknown
801	1.0865	1.1279	1.0651	1.2945	1.2139	7	AL11, fused gene from chromosome 1q
802	0.9384	0.8887	0.7456	1.2847	1.0899	7	protein tyrosine phosphatase, receptor type, B
803	0.9298	0.8771	0.7621	1.1161	0.8372	7	RIKEN cDNA, 27000551607 gene
804	1.0172	0.9334	0.8731	1.4073	1.1697	7	RIKEN cDNA, 27000551607 gene
805	1.0252	1.0214	0.9262	1.3605	1.1665	7	RIKEN cDNA, 1110005N04 gene
806	1.1757	1.1622	1.1274	1.4591	1.3171	7	hypothetical protein, MGC-56957
807	1.1705	1.1709	1.1608	1.4591	1.0748	8	hypothetical protein, L41
808	1.0635	1.3540	1.4143	1.0984	0.9137	8	lysophosphatidylcholine acyltransferase
809	1.0256	1.3059	1.4143	1.0984	0.9137	8	3-phosphoglycerate dehydrogenase
810	1.0346	1.3531	1.4143	1.0984	1.0462	8	nucleic acid sensitive element binding protein 1
811	0.9787	1.3531	1.4143	1.0984	1.0462	8	Unknown
812	1.0556	1.2144	1.2463	1.1075	0.9729	8	fragile histidine triad gene
813	1.0556	1.2144	1.2463	1.1075	1.0754	8	RIKEN cDNA, 120001493 gene
814	0.9228	1.2748	1.3250	1.2011	1.1393	8	forhead box M1
815	0.9803	1.1853	1.5148	1.0335	0.9811	8	secreted phosphoprotein 1
816	1.1463	1.4757	1.8329	2.3798	1.3904	8	secreted phosphoprotein 1
817	1.0634	1.4566	1.6696	1.4566	1.2921	8	phospholipase L36
818	0.9823	1.2645	1.4028	1.1183	1.0792	8	retinol-binding protein 7
819	0.9367	1.4419	1.5893	1.1107	1.0894	8	retinol-binding protein 7
820	0.7917	1.6376	1.8312	1.0976	0.9740	8	FK-506 binding protein 10 (65 kDa)
821	1.0398	2.4542	2.5246	1.0864	1.2043	8	hemoglobin (deacylating) 1
822	1.0398	2.4542	2.5246	1.0864	1.0692	8	high mobility group AT-hook 1
823	1.0483	1.3901	1.2959	1.1152	1.1263	8	inhibin beta-B
824	0.9601	1.1952	1.2959	0.9994	1.0090	8	myeloid-associated differentiation marker
825	1.0409	1.4028	1.5614	1.1026	1.1820	8	RIKEN cDNA 1300019121 gene
826	1.0368	1.4028	1.5614	1.1026	1.1820	8	protein phosphatase 1, catalytic subunit, alpha isoform
827	0.9552	1.2344	1.3381	1.0867	1.2622	8	unknown
828	1.2389	1.2774	1.4450	1.0867	1.1517	8	enhancer of zeste homologue 2 (Drosophila)
829	0.9267	1.2192	1.6018	0.9633	1.1240	8	CCU1-binding protein
830	1.1364	1.3409	1.4842	1.1054	0.9769	8	CCU1-binding protein
831	1.1178	1.3461	1.5230	1.0800	0.9605	8	ESTER cDNA, 2600017H24 gene
832	1.0265	1.2562	1.3312	1.0744	1.0905	8	RIKEN cDNA 111005A24 gene
833	0.9568	1.1392	1.1923	0.9076	1.0800	8	muscle homologue 6 (E. coli)
834	0.9568	1.1392	1.1923	0.9076	0.8956	8	TRAF-interacting protein
835	0.9733	1.1567	1.2001	0.9746	0.9198	8	eyelin EI

836	0.9535	1.2877	1.3981	0.9579	0.8719	8	RIKEN cDNA 181065K22 gene
837	0.9752	1.5091	1.6571	1.0736	1.0018	8	erythroid differentiation regulator
838	0.9263	1.2611	1.2404	0.9111	0.9423	8	calcitonin receptor-like receptor 4 (S. cerevisiae)
839	1.0243	1.2567	1.2798	0.9981	0.9792	8	RIKEN cDNA 62157D05 gene
840	0.9986	1.2793	1.3604	1.0654	1.0846	8	RNA capping enzyme 2
841	1.1115	1.2650	1.3067	1.1022	1.1182	8	NA-actin-binding protein kinase
842	1.0186	1.1358	1.1682	1.0152	1.0184	8	synaptobin, basic 2
843	1.0902	1.2473	1.2036	1.1692	1.1034	8	ESTs
844	0.9552	1.2053	1.2003	0.9815	0.9815	8	RIKEN cDNA 3326402E02 gene
845	0.9752	1.4399	1.2713	1.1845	0.9904	8	karvogenin (uniprot) beta 3
846	0.7846	0.8672	0.8370	0.8170	0.7820	8	ESTs, weakly similar to MAJOR URINARY PROTEIN 4 PRECURSOR (M. musculus)
847	1.0338	2.0784	1.7794	1.4405	1.0162	8	RIKEN cDNA 261030D06 gene
848	1.0881	1.3247	1.4167	1.2938	1.0599	8	mini chromosome maintenance deficient 2 (S. cerevisiae)
849	0.9663	1.4189	1.3009	1.1512	1.0359	8	SW/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5
850	0.8998	1.6631	1.5009	1.1670	0.9235	8	mini chromosome maintenance deficient 2 (S. cerevisiae)
851	0.9813	1.3582	1.2973	1.1468	0.9982	8	ESTs, weakly similar to TYROSINE-PROTEIN KINASE JAK3 (M. musculus)
852	0.9157	1.3667	1.3004	1.1916	0.9332	8	Unlabeled
853	0.9737	1.4200	1.3047	1.2093	1.0386	8	uniprotin
854	0.9585	1.3977	1.2746	1.2102	1.0387	8	uniprotin
855	1.0123	1.3805	1.3073	1.2457	1.2033	8	RIKEN cDNA 2510015F01 gene
856	0.9089	1.4183	1.2457	1.1461	1.0663	8	proteasome 1
857	0.9256	1.4183	1.2254	1.0872	1.0790	8	regulator for ribosome resistance homolog (S. cerevisiae)
858	0.9256	1.2509	1.1873	1.0990	1.0063	8	damage specific DNA binding protein 1 (127 kDa)
859	1.0299	1.3535	1.2718	1.2333	1.0826	8	myosin Ic
860	1.0571	1.3370	1.3444	1.2004	1.0226	8	FK506 binding protein 1a (12 kDa)
861	0.9983	1.3675	1.4768	1.1448	1.0226	8	apartine/aprimidine endonuclease
862	1.0526	1.3638	1.3916	1.1274	1.0620	8	RIKEN cDNA 693054D03 gene
863	0.8926	1.4296	1.2322	0.9500	0.8629	8	expressed sequence AA409944
864	1.0256	1.3651	1.3109	1.0412	0.9988	8	RIKEN cDNA 0610041B09 gene
865	1.0822	1.9930	1.6940	1.1583	0.9855	8	cyclin-dependent kinase inhibitor 1A (P21)
866	0.9237	1.5163	1.3416	0.9375	0.8375	8	DNA methyltransferase (cytosine-5)
867	1.1364	1.7778	1.9225	1.3915	1.0715	8	expressed sequence AL02737
868	0.9705	1.3248	1.3714	1.0729	0.9268	8	private kinase 5
869	0.9647	1.1680	1.1923	1.0338	0.9406	8	private kinase 5
870	0.9876	1.1944	1.2588	1.1053	0.9482	8	UDP-Galactose 4-epimerase
871	0.9515	1.4453	1.5141	1.2588	0.9448	8	serum amyloid A 3
872	1.1114	2.2702	1.9445	1.2738	0.8902	8	serum amyloid A 3
873	0.8893	1.3300	1.3415	1.0710	0.9710	8	reticulolysosomal factor 3
874	1.1208	1.8190	1.8661	0.9826	0.8612	8	reticulolysosomal factor 3, subunit 4 (delta, 44 kDa)
875	1.1830	1.5507	1.3841	1.2287	0.9901	8	mini chromosome maintenance deficient (S. cerevisiae)
876	0.8906	1.4498	1.2272	1.0730	1.1306	8	ribosomal protein S26
877	0.9239	1.7468	1.4637	1.1897	1.0778	8	phospholipid scramblase 1
878	1.0331	3.7822	2.8146	1.7527	1.7093	8	RIKEN cDNA 061001610 gene
879	0.9542	1.4141	1.2747	1.1096	1.0919	8	S100 calcium binding protein A10 (calpactin)
880	0.9242	1.4141	1.2747	1.1096	1.0919	8	S100 calcium binding protein A10 (calpactin)

881	0.9461	1.7827	1.2855	1.2276	1.1364	8	group specific component
882	0.8998	1.5321	1.2290	1.1541	1.0309	8	Macrophages. Similar to hypodermal protein FLP0335, clone MGC28912 IMAGE:492274.
883	0.9879	2.0388	1.5224	1.3116	1.2219	8	mRNA, complete cds
884	1.0047	2.0935	1.7301	1.4719	1.2822	8	colony stimulating factor 1 (macrophage)
885	0.9698	2.1108	1.6417	1.3894	1.1897	8	cold shock domain protein A
886	0.9661	1.7208	1.4167	1.2155	1.1198	8	flotillin 1
887	0.9238	1.6345	1.3168	1.0144	1.1043	8	enteryotic translation initiation factor 5A
888	0.9238	1.6345	1.3168	1.0144	1.1043	8	NIMA (never in mitosis gene) related expressed kinase 6
889	0.9199	1.9203	1.3751	1.1123	1.0799	8	G1 to phase transition 1
890	0.9483	2.3592	1.6048	1.3659	1.0729	8	chaperonin subunit 3 (panna)
891	0.9730	1.7194	1.3046	1.0652	1.0799	8	RIKEN cDNA 261035D13 gene
892	1.0604	1.7694	1.6202	1.1721	1.2007	8	thioredoxin-like (32413)
893	1.0014	1.4278	1.2144	1.0377	1.0589	8	headpoint cluster region protein 1
894	0.7965	1.2243	1.1858	0.8377	0.8802	8	SHC (structural maintenance of chromosomes 1)-like 1 (S. cerevisiae)
895	1.0803	1.3750	1.3074	1.1710	1.1862	8	Kruppel-like factor 5
896	1.0082	1.3212	1.2504	1.0867	1.0966	8	RIKEN cDNA 251000A17 gene
897	0.9992	1.6277	1.1318	1.0470	1.0547	8	RIKEN cDNA 251000A17 gene
898	0.9447	1.2588	1.2104	1.0200	1.0341	8	RIKEN cDNA 1110003H02 gene
899	1.0011	2.0612	1.3058	1.0143	1.0631	8	RIKEN cDNA 5410416A05 gene
900	0.9157	1.4013	1.3559	0.9555	1.1175	8	expressed sequence R75232
901	0.8112	1.3552	1.2566	0.8814	1.1199	8	platelet derived growth factor receptor, beta polypeptide
902	0.8242	1.3552	1.2566	0.8814	1.1199	8	exportin 1, CRM1 homolog (yeast)
903	0.8242	1.3552	1.2566	0.8814	1.1199	8	adenylosuccinate synthetase 2, non muscle
904	1.0760	1.2433	1.1610	1.0387	1.0001	8	crystallin, alpha B
905	0.8533	1.4897	1.1450	0.9054	0.7761	8	peroxiredoxin 5
906	0.9973	1.7128	1.3332	1.0895	0.8870	8	glutathione S-transferase, mu 6
907	0.9213	1.3955	1.2021	0.9890	0.9673	8	PS1
908	0.9483	1.7476	1.3518	1.0398	0.9622	8	Mus musculus, clone M-AGE-44862/65, mRNA, partial cds
909	0.9587	3.3629	1.8313	1.1715	1.0554	8	PS1
910	0.9659	1.3942	1.1693	1.0673	0.9685	8	PS1
911	0.9554	1.7080	1.2838	1.1494	1.0259	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
912	0.9236	1.7544	1.2779	1.1024	0.9585	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
913	1.6719	3.3827	2.0004	0.9177	0.790	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
914	0.9191	1.8726	1.2456	0.9584	0.9707	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
915	1.0491	1.7138	1.2456	0.9584	0.9707	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
916	1.0389	1.3102	1.3410	1.0644	1.0835	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
917	0.9483	1.3518	1.2753	0.9012	1.2202	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
918	0.9483	1.3518	1.2753	0.9012	1.2202	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
919	0.9483	1.3518	1.2753	0.9012	1.2202	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
920	0.9265	1.2615	1.2228	0.9098	1.1680	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
921	1.0015	1.1566	1.2123	0.9398	1.0363	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
922	1.0089	1.2420	1.2912	1.0800	1.1813	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
923	0.9884	1.2165	1.2276	0.9395	1.0978	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
924	0.9563	1.2095	1.2477	0.9184	1.0629	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)
925	1.0527	1.3395	1.1731	0.9617	1.0150	8	PS1. Moderately similar to T00381 (KLA0063) protein (H.sapiens)

926	0.9314	1.3143	1.1483	0.8630	0.9104	8	spermatogenesis associated factor
927	0.8097	2.0123	1.3849	0.7516	0.8230	8	phospholipase A2, group IB, pancreatic
928	1.0119	1.4082	1.2014	0.9940	1.0221	8	proteasome (prosome, macropain) 20S subunit, non-ATPase, 13
929	1.0211	1.2430	1.1788	0.9232	0.9643	8	RIKEN cDNA 0610071D1 gene
930	1.0922	1.4011	1.3576	0.9118	0.9694	8	tumor necrosis factor receptor superfamily, member 10b
931	0.9632	2.3385	1.4739	0.6976	0.7120	8	metallothionein 1
932	1.1409	1.4503	1.2784	0.8595	0.8595	8	RIKEN cDNA 181003B15 gene
933	1.0397	1.5167	1.3107	0.9042	0.9042	8	MYD88-binding protein (P160) 1a
934	1.0783	1.4443	1.3446	0.9042	0.9042	8	N-acetylphosphate pyruvate lyase
935	1.0443	1.4443	1.3446	0.9042	0.9042	8	actin related factor 2
936	1.0222	1.3169	1.1789	0.9739	1.1521	8	poly(GC) binding protein 1
937	1.0415	1.4282	1.2706	0.9824	1.1195	8	heart shock 70 kDa protein 4
938	1.0332	1.4662	1.3097	0.9474	1.1177	8	RIKEN cDNA 2810409107 gene
939	1.0604	1.4091	1.2679	1.0375	1.1612	8	CDK2 (cyclin-dependent kinase 2)-associated protein 1
940	1.0057	1.2417	1.1350	0.9895	1.0433	8	RIKEN cDNA 2310079C17 gene
941	1.1422	1.4354	1.3050	0.9770	1.1061	8	poliovirus receptor-related 3
942	0.9717	1.2575	1.2031	0.9203	1.0098	8	RIKEN cDNA 0704631B02 gene
943	1.0338	1.3252	1.2681	0.9331	1.0866	8	ESTs
944	1.0070	1.3308	1.2793	0.8952	1.0254	8	RIKEN cDNA 281004N23 gene
945	0.8562	0.9086	0.6539	0.7555	0.6474	9	acyl-Coenzyme A dehydrogenase, very long chain
946	0.9051	0.8925	0.7442	0.7410	0.6812	9	signaling intermediate in Toll pathway-evidently conserved
947	0.8913	0.8476	0.6680	0.7459	0.5878	9	Unknown
948	0.6959	0.2637	0.2559	0.4656	0.4656	9	Cytokeratin 8-50, 2-4
949	0.8439	0.7078	0.6559	0.8327	0.8473	9	cellular endothelial growth factor A
950	0.8439	0.7078	0.6559	0.8327	0.8473	9	response 1
951	1.0198	0.8330	0.6820	0.7713	0.7476	9	upstream transcription factor 1
952	0.8984	0.7274	0.5571	0.6259	0.6831	9	Mus musculus, Similar to KIAA1075 protein, clone IMAGE:509327, mRNA, partial cds
953	0.9912	0.9011	0.8155	0.8613	0.8507	9	ESTs
954	1.0566	0.8549	0.6306	0.7014	0.6514	9	Unknown
955	0.9210	0.7784	0.5715	0.6506	0.6378	9	expressed sequence AW61723
956	1.1198	0.9949	0.6888	0.8164	0.7860	9	ESTs
957	0.9687	0.8107	0.7639	0.7686	0.6485	10	RIKEN cDNA 1700019P13 gene
958	0.9378	0.8541	0.8934	0.7945	0.7153	10	polymers, gamma
959	1.1040	0.9020	0.7961	0.5188	0.3867	10	growth arrest and DNA-damage-inducible 45 gamma
960	0.8252	0.8038	0.7707	0.7536	0.6861	10	Unknown
961	1.0298	0.8656	0.8640	0.7991	0.8070	10	single Ig IL-1 receptor related protein
962	1.0620	0.5556	0.5847	0.4352	0.4283	10	sex-delta interactor immunob (Phosphila)
963	0.8831	0.5946	0.6819	0.7061	0.6819	10	sex-delta interactor immunob (Phosphila)
964	0.9305	0.5359	0.5859	0.7061	0.7061	10	sex-delta interactor immunob (Phosphila)
965	1.0169	0.8792	0.6832	0.5737	0.7986	10	Unknown
966	1.0497	0.8456	0.7612	0.7490	0.5496	10	UDP-glucose-6-epimerase 1 family, member 1
967	1.0497	0.8456	0.7612	0.7490	0.5496	10	D-amino acid oxidase
968	1.0244	0.9427	0.8750	0.7907	0.8257	10	RIKEN cDNA 6330411B15 gene
969	0.9882	0.8769	0.8026	0.8647	0.8679	10	expressed sequence AB61919
970	1.1131	0.8263	0.8425	0.7617	0.7845	10	f-box only protein 3
971	0.9528	0.5563	0.6746	0.5572	0.4357	10	cytochrome c oxidase, subunit VIIa
							glutamine synthetase



972	1.2090	0.7128	0.9213	0.7013	0.5613	10	FXVD domain-containing ion transport regulator 2
973	1.0048	0.7884	0.7990	0.7590	0.6439	10	DNA segment, Chr 10, Wayne State University 181, expressed
974	0.8833	0.7048	0.7194	0.6722	0.6111	10	cytosolic carrier family 1 (cationic amino acid transporter, y <sup>+</sup> system), member 7
975	1.0050	0.8164	0.8458	0.7760	0.6538	10	glutamine synthetase
976	0.7740	0.4108	0.8426	0.7357	0.6334	10	transmembrane protein 8 (five membrane-spanning domain)
977	0.9002	0.7412	0.7884	0.6446	0.6328	10	cytochrome P450, 2A9
978	1.1106	0.7079	0.9261	0.6956	0.7315	10	solute carrier family 25 (mitochondrial carrier, adenine nucleotide translocator), member 13
979	0.9594	0.8183	0.9159	0.7133	0.7878	10	expressed sequence A595924
980	0.9708	0.8352	0.9121	0.7053	0.8224	10	hydroxytetraol 17-beta dehydrogenase 7
981	0.9708	0.8352	0.9121	0.7053	0.8224	10	histone gene complex 2
982	1.0054	0.7926	0.9405	0.6884	0.8122	10	Mus musculus, clone MGC-18871 IMAGE424793, mRNA, complete cds
983	0.8737	0.7926	0.8300	0.6773	0.7674	10	amphiphilic 12-hydroxyoctene, perolefine 2
984	1.2340	0.9877	1.0330	0.7811	0.7963	10	unregulated during skeletal muscle growth 5
985	1.0932	0.8639	0.9127	0.7586	0.5608	10	Unknown
986	1.0165	0.8971	0.9690	0.6225	0.6251	10	gap junction membrane channel protein beta 2
987	1.0450	0.9308	0.8611	0.6815	0.6822	10	alcohol dehydrogenase (class II), pi isoenzyme
988	0.9026	0.8951	0.6761	0.5261	0.4492	10	muscle monomer 1 in hypodermis protein MGC4368, clone MGC28978 IMAGE430381, mRNA, complete cds
989	1.0225	0.9839	0.8840	0.7646	0.7836	10	RNA, complete cds
990	0.9775	0.8444	0.7487	0.6177	0.6206	10	S-adenosylhomocysteine hydrolase
991	0.9271	0.9294	0.6886	0.6177	0.5416	10	period homolog 1 (Drosophila)
992	0.9664	0.9156	0.7310	0.6243	0.5416	10	EST1, Moderately similar to SEC7 homolog (Homo sapiens) (H.sapiens)
993	0.9586	0.9156	0.7310	0.6243	0.5416	10	EST1, Moderately similar to SEC7 homolog (Homo sapiens) (H.sapiens)
994	0.8393	0.9486	0.8363	0.6518	0.7229	10	hepatite nuclear factor 4
995	0.8393	0.9486	0.8363	0.6518	0.7229	10	macrophage migration inhibitory factor
996	0.9571	0.9154	0.8538	0.6816	0.7615	10	neuronal precursor cell expressed, developmentally down-regulated gene 4a
997	0.9200	0.8715	0.8370	0.7089	0.7528	10	serine hydroxymethyl transferase 1 (bottle)
998	1.0673	1.0749	0.9741	0.7741	0.7832	10	DNA segment, Chr 3, Wayne State University 31, expressed
999	0.9406	0.9407	0.8580	0.7114	0.7832	10	serum glucocorticoid regulated kinase
1000	1.0031	0.9089	0.7904	0.7543	0.9717	11	MG-123 related protein MGC1237 similar to ribosomal protein S6 kinase, clone MGC28978 IMAGE430381, mRNA, complete cds
1001	0.9025	0.8411	0.7798	0.7633	0.8986	11	Mus musculus, hypodermis, clone MGC357217, mRNA, complete cds
1002	1.0356	0.7156	0.7595	0.5273	0.8067	11	EST1, similar to I77132 Na <sup>+</sup> -dependent vitamin C (H.sapiens)
1003	0.9586	0.8592	0.6928	0.7492	0.8855	11	CEA-related cell adhesion molecule 2
1004	0.9311	0.8195	0.6879	0.6942	0.8176	11	Mus musculus, clone IMAGE338777, mRNA, partial cds
1005	0.8659	0.6873	0.7813	0.9056	1.0118	11	low density lipoprotein receptor-related protein 6
1006	1.0417	0.8783	0.8783	0.9056	1.0118	11	EST1
1007	0.9358	0.6338	0.6314	0.6337	0.8084	11	acyl-Coenzyme A dehydrogenase, short/branched chain
1008	0.9453	0.8301	0.8198	0.7384	0.8614	11	RIKEN cDNA 231004403 gene
1009	1.0184	0.6622	0.6123	0.3889	0.8067	11	ATPase, H <sup>+</sup> -transporting, lysosomal (vacuolar proton pump), alpha 70 kDa, isoform 1
1010	1.0184	0.6622	0.6123	0.3889	0.8067	11	ATPase, H <sup>+</sup> -transporting, lysosomal (vacuolar proton pump), alpha 70 kDa, isoform 1
1011	1.0905	0.8205	0.7908	0.7760	0.9682	11	superoxide dismutase 2, mitochondrial
1012	1.0518	0.6570	0.5914	0.5503	0.9616	11	RIKEN cDNA DK3000215 gene
1013	0.8270	0.6440	0.6076	0.4833	0.7900	11	arapom 2
1014	0.9791	0.6898	0.7041	0.9938	0.9095	11	CEA-related cell adhesion molecule 1
1015	0.9384	0.7774	0.7389	0.7022	0.9073	11	expressed sequence A104468
							ATPase, H <sup>+</sup> /K <sup>+</sup> -transporting, alpha polypeptide

1016	1.1805	0.7019	0.5323	0.4116	0.7665	11	calbindin-D28K
1017	0.9568	0.8992	0.8657	0.7889	0.9885	11	RIKEN cDNA 903612K14 gene
1018	0.9356	0.7407	0.7119	0.6882	0.8112	11	ESTs
1019	1.0822	0.7842	0.7402	0.6598	0.8358	11	cytochrome c oxidase, subunit Vc
1020	1.1006	0.7344	0.7024	0.6204	0.8251	11	AU RNA binding protein/enoyl-coenzyme A hydratase
1021	0.9835	0.8374	0.8166	0.7378	0.9034	11	prohibitin
1022	0.9925	0.7927	0.7053	0.6264	0.7778	11	RIKEN cDNA 270043J08 gene
1023	0.9742	0.8927	0.7953	0.6972	0.8791	11	dopa decarboxylase
1024	1.0160	0.7680	0.7377	0.7021	0.8604	11	ESTs, Weakly similar to ADT1 MOUSE ADP-ATP CARRIER PROTEIN, HEPA2/HEP2B ETAL MUSCLE ISOFORM T1 (M.musculus)
1025	1.0466	0.9330	0.8966	0.8304	0.9389	11	expressed sequence A1173 ROSINSE-PROTEIN KINASE JAK3 (M.musculus)
1026	0.9460	0.7150	0.6676	0.6305	0.7530	11	ESTs, Weakly similar to kinase 3
1027	0.9886	0.8343	0.7855	0.7388	0.8472	11	PC1 A162-membranous
1028	0.6974	0.4804	0.4424	0.3964	0.4752	11	homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member
1029	0.9916	0.7285	0.6752	0.6177	0.7692	11	salivary carrier family 22 (organic cation transporter), member 4
1030	0.9625	0.7216	0.6521	0.5149	0.6562	11	RIKEN cDNA 953089B04 gene
1031	0.9471	0.7616	0.6508	0.5787	0.6966	11	solute carrier family 26, member 4
1032	0.9952	0.7110	0.5728	0.4358	0.5965	11	tail-1 protein 6
1033	0.9922	0.7903	0.7121	0.6480	0.7357	11	expressed sequence A1504961
1034	0.9609	0.8559	0.8063	0.6809	0.7884	11	expressed sequence AV046379
1035	0.9811	0.8559	0.8063	0.7762	0.8606	11	ESTs
1036	0.9811	0.8559	0.8063	0.7762	0.8606	11	sideoflexin 1
1037	0.9864	0.8172	0.7755	0.6381	0.9205	11	RIKEN cDNA 513340J05 gene
1038	0.8703	0.7712	0.7184	0.6293	0.8410	11	RIKEN cDNA 150064J02 gene
1039	0.8965	0.8619	0.7684	0.7419	0.7980	11	private kinase Iyer and Rubin 4
1040	1.0614	1.0054	0.6685	0.5872	0.7662	11	glutathione S-transferase 1 (Drosophila)
1041	0.8833	0.7591	0.6519	0.6345	0.7619	11	heat shock protein, 105 kDa
1042	0.7851	0.7654	0.7095	0.7205	0.7495	11	expressed sequence AB444876
1043	0.9252	0.9021	0.7695	0.6509	0.8532	11	kinase family member 21A
1044	0.9903	0.9088	0.8075	0.7381	0.8449	11	expressed sequence AB444876
1045	0.9834	0.9108	0.8079	0.7134	0.8449	11	RIKEN cDNA 2410002J21 gene
1046	1.0546	1.0447	1.3198	1.3130	1.0548	12	proteasome (prosome, macropain) subunit, alpha type 2
1047	1.0710	1.3929	1.3312	1.6800	1.1465	12	mannosine monophosphate reductase
1048	1.2601	1.6010	1.3318	1.5547	1.0281	12	glutathione S-transferase, p2
1049	1.1352	1.7983	1.4772	1.3992	1.0924	12	DNA methyltransferase 3B
1050	1.0400	1.4678	1.3195	1.5447	1.0924	12	major vault protein
1051	0.9338	1.7313	1.3415	1.6079	1.1286	12	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 1
1052	0.9338	1.4280	1.2887	1.4485	1.3069	12	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 1
1053	0.9169	1.4190	1.2861	1.4841	1.2482	12	cellular translation initiation factor 3
1054	0.9291	1.2736	1.2138	1.3638	1.1878	12	glutathione S-transferase 1 (Drosophila)
1055	0.9989	1.7824	1.4076	1.8025	1.2388	12	ESTs
1056	0.9763	1.4053	1.2160	1.5757	1.1421	12	mannosine monophosphate maintenance deficient 7 (S. cerevisiae)
1057	0.9783	1.9044	1.5219	2.0547	1.2060	12	mannosine monophosphate maintenance deficient 7 (S. cerevisiae)
1058	1.0115	1.3461	1.2286	1.5920	1.1570	12	RIKEN cDNA 250001N01 gene

1059	1.1335	1.6446	1.4540	1.7949	1.3646	12	Unknown
1060	1.0333	1.5936	1.5660	1.8599	1.3577	12	Ribosomal protein L29
1061	1.0396	1.7188	2.3830	1.4948	1.4948	12	has homolog 2 in IV, alpha 1
1062	1.1069	2.1966	1.9482	2.6636	1.7530	12	collagenase, clone IMAGE3494258, mRNA, partial cds
1063	1.0359	1.6490	1.4289	1.6658	1.7701	13	5' UTR, noncoding exon only
1064	1.0548	1.2997	1.2611	1.3461	1.2371	12	S' melittase, cytosolic
1065	1.1342	1.3235	1.3444	1.4977	1.1073	12	apoptosis inhibitory protein 5
1066	0.9434	1.3235	1.3444	1.4977	1.1073	12	WTC-associated zinc finger protein (uridine-binding transcription factor)
1067	0.9434	1.3235	1.3444	1.4977	1.1073	12	lysine 3-monooxygenase/histone H3 5-monooxygenase activation protein, epsilon polypeptide
1068	0.9794	1.3235	1.3444	1.4977	1.1073	12	RIKEN cDNA 0930579A.11 gene
1069	1.0688	1.4107	1.3574	1.4379	1.1426	12	Mus musculus, Similar to hypothetical protein DKZp566A.154, clone MGC:18989
1070	1.0384	1.7156	1.6628	1.7704	1.2620	12	IMAGE401217, mRNA, complete cds
1071	1.0272	1.6670	1.5489	1.7059	1.2080	12	cardiac responsive adjuvant protein
1072	1.0938	1.2541	1.2956	1.4300	1.1461	12	cardiac responsive adjuvant protein
1073	1.0534	1.2717	1.2368	1.3883	1.1354	12	procollagen lysine 2-oxoglutarate 5-oxoglutarate 2
1074	1.051	1.2767	1.2656	1.3783	1.1899	12	serine protease inhibitor, Kunitz type 2
1075	1.0318	1.6563	1.7177	2.0415	1.3179	12	ratine sarcoma oncogene
1076	1.0236	1.2391	1.2952	1.4582	1.1544	12	Ribosomal protein S4
1077	0.7752	1.4606	0.9529	1.9073	1.2574	12	collagen and elastin binding protein
1078	0.8561	1.6469	1.0541	2.0671	1.3573	12	collagen type II
1079	1.0533	1.3540	1.3540	1.4041	1.1624	12	procollagen, type IV, alpha 2
1080	0.9961	1.3763	1.1500	1.3201	1.1786	12	cathepsin L
1081	1.1691	1.7019	1.2211	1.4683	1.3352	12	cathepsin L
1082	0.7786	0.7212	0.7562	0.7626	0.5820	12	integrin alpha 6
1083	0.8123	0.8600	0.8316	0.8140	0.6928	13	RIKEN cDNA 1300013F15 gene
1084	0.8480	0.9504	0.7898	0.7952	0.5793	13	ChyP300-interacting transactivator with Glu/Asp-rich carboxy-terminal domain 1
1085	0.9117	1.0288	1.3129	0.9637	1.1158	14	zinc finger like protein 1
1086	0.9117	1.0288	1.3129	0.9637	1.1158	14	ubiquitin-like 1
1087	1.0415	1.2394	2.1900	1.3649	1.6645	14	S100 calcium binding protein A4
1088	1.0117	1.1399	1.3869	1.1813	1.2944	14	neurofilament cytosolic factor 2
1089	0.7711	1.2084	0.5412	1.5063	1.9526	14	neurofilament cytosolic factor 2
1090	1.0400	1.3467	1.7054	2.3555	1.2895	14	interferon activated gene 29
1091	1.0369	1.1560	1.2849	1.1009	1.1142	14	RIKEN cDNA 201218F06 gene
1092	1.0276	1.1616	1.3901	1.0470	1.1142	14	RNA gene, partial cds
1093	1.1397	1.3345	1.4498	1.3345	1.2991	14	light chain polypeptide (Lca)
1094	0.0055	1.1348	1.1669	1.1669	1.1833	14	SCC61, gamma subunit (S. cerevisiae)
1095	0.9610	1.1348	1.2628	1.2628	1.1833	14	doublet cortex and calcitonin/calcimodulin-dependent protein kinase-like 1
1096	0.9610	1.2976	1.2208	1.3368	1.2993	14	radical oxidant
1097	0.9880	1.1557	1.3407	1.2361	1.4099	14	Unknown
1098	1.0192	1.3749	1.7257	1.1649	1.1829	14	expressed sequence AW413625
1099	0.9773	1.5072	2.0022	1.3664	1.5915	14	hematological and neurological expressed sequence 1
1100	0.9548	1.2515	2.2390	1.0730	1.0596	14	epithelial membrane protein 3
1101	1.0535	1.1962	1.7605	1.1520	1.1549	14	thymidine kinase 1
1102	1.0410	1.0896	1.3744	1.0873	1.0573	14	RIKEN cDNA 1110038J14 gene
1103	1.1411	1.2914	2.6723	1.5075	1.0320	14	cathepsin Z
						14	post division cycle 2 homolog A (S. pombe)

1104	1.1579	1.1821	1.6573	1.1931	1.0737	14	CD23 protein kinase 1
1105	0.9318	1.0360	1.8331	1.4314	1.2641	14	expressed sequence A449309
1106	1.1991	1.2134	1.5060	1.3744	1.2615	14	bone marrow stromal cell antigen 1
1107	1.0601	1.2620	2.0800	1.7850	1.2532	14	bone marrow stromal cell antigen 2
1108	0.9925	1.1426	3.4319	1.7680	1.2615	14	interleukin-10 receptor
1109	1.0539	1.1309	2.6941	1.8780	1.0592	14	interleukin-10 receptor
1110	0.9530	1.1300	2.6941	1.8780	1.0592	14	ESR3, Weekly similar to limb expression 1 homolog (chicken) (M. musculus) (M. musculus)
1111	0.9436	1.1337	2.6941	1.8780	1.0592	14	ESR3, Weekly similar to limb expression 1 homolog (chicken) (M. musculus) (M. musculus)
1112	0.9436	1.1337	2.6941	1.8780	1.0592	14	ESR3, Weekly similar to limb expression 1 homolog (chicken) (M. musculus) (M. musculus)
1113	0.9436	1.1337	2.6941	1.8780	1.0592	14	ESR3, Weekly similar to limb expression 1 homolog (chicken) (M. musculus) (M. musculus)
1114	0.9436	1.1337	2.6941	1.8780	1.0592	14	ESR3, Weekly similar to limb expression 1 homolog (chicken) (M. musculus) (M. musculus)
1115	0.9003	1.0715	1.3528	1.1319	1.0338	14	TEA domain family member 2
1116	1.0515	1.1979	1.8263	1.3929	1.2170	14	pyridoxal (pyridoxine, vitamin B6) kinase
1117	0.9140	1.0785	1.2413	1.0728	1.3265	15	A kinase (PKC $\alpha$ ) nuclear protein 2
1118	0.9704	1.0785	1.2413	1.0728	1.3265	15	protein tyrosine phosphatase 4b1
1119	1.0255	1.8462	1.2927	1.1698	1.1375	15	serine-arginine repeatase matrix 1
1120	1.0495	1.3650	1.1613	1.0815	1.0684	15	serine-arginine repeatase matrix 1
1121	0.9533	1.5063	1.3774	1.7003	1.0684	15	serine-arginine repeatase matrix 1
1122	0.9473	1.2334	1.2088	1.0737	1.2283	15	serine-arginine repeatase matrix 1
1123	0.9000	1.0514	1.2555	1.0651	1.1448	15	serine-arginine repeatase matrix 1
1124	1.0278	1.2534	1.1622	1.0815	1.0684	15	serine-arginine repeatase matrix 1
1125	1.0268	1.2534	1.1622	1.0815	1.0684	15	serine-arginine repeatase matrix 1
1126	1.0268	1.2534	1.1622	1.0815	1.0684	15	serine-arginine repeatase matrix 1
1127	1.0188	1.1930	1.1767	1.1366	1.2544	15	serine-arginine repeatase matrix 1
1128	0.9902	1.3344	1.2604	1.0297	1.1650	15	serine-arginine repeatase matrix 1
1129	0.9216	1.1940	1.1093	0.9664	1.1152	15	serine-arginine repeatase matrix 1
1130	0.9093	1.3225	1.2436	0.9681	1.2763	15	serine-arginine repeatase matrix 1
1131	0.9979	1.2759	1.1970	1.0145	1.2187	15	serine-arginine repeatase matrix 1
1132	0.8501	1.3359	1.1779	1.0009	1.2015	15	serine-arginine repeatase matrix 1
1133	0.9389	1.3929	1.1776	1.0123	1.2458	15	serine-arginine repeatase matrix 1
1134	1.0172	1.1777	1.2130	1.0220	1.1922	15	serine-arginine repeatase matrix 1
1135	1.0058	1.1785	1.1752	0.9891	1.1682	15	serine-arginine repeatase matrix 1
1136	1.0015	1.2492	1.1454	1.0197	1.3066	15	serine-arginine repeatase matrix 1
1137	0.9485	1.1812	1.1673	0.9851	1.2453	15	serine-arginine repeatase matrix 1
1138	0.9893	1.1928	1.1357	0.9582	1.2453	15	serine-arginine repeatase matrix 1
1139	0.8586	1.0475	0.9142	0.8582	0.9788	15	serine-arginine repeatase matrix 1
1140	0.9742	1.0475	0.9142	0.8582	0.9788	15	serine-arginine repeatase matrix 1
1141	0.9436	1.1337	2.6941	1.8780	1.0592	15	serine-arginine repeatase matrix 1
1142	0.9436	1.1337	2.6941	1.8780	1.0592	15	serine-arginine repeatase matrix 1
1143	0.9003	1.0715	1.3528	1.1319	1.0338	15	serine-arginine repeatase matrix 1
1144	0.9671	1.0243	0.8303	0.8069	1.0288	15	serine-arginine repeatase matrix 1
1145	1.1326	1.0243	0.9914	1.1795	1.2983	15	serine-arginine repeatase matrix 1
1146	0.7944	0.7365	0.6909	0.8202	0.9165	15	serine-arginine repeatase matrix 1
1147	0.9515	0.8055	0.7684	0.9505	1.1355	15	serine-arginine repeatase matrix 1
1148	0.9551	0.8270	0.8153	1.0046	1.2762	15	serine-arginine repeatase matrix 1
1149	1.0462	0.8143	0.7505	1.1385	1.1028	15	serine-arginine repeatase matrix 1

1150	0.9734	0.8566	0.8087	1.0005	1.0230	16	topoisomerase (DNA III beta)
1151	0.9391	0.8452	0.7943	1.0388	1.0228	16	Mus musculus, clone MGC-37560 IMAGE:6987746, mRNA, complete cds
1152	0.9457	0.7893	0.6889	1.0771	1.1442	16	retrotransposon, 1000 bp, human, alien, missing type information regulation 2 homolog 7 (S. pombe)
1153	0.9818	0.8115	0.7371	1.0933	1.1716	16	retrotransposon, 1000 bp, human, alien, missing type information regulation 2 homolog 7 (S. pombe)
1154	0.9276	0.6977	0.6572	0.9335	0.9746	16	retrotransposon, 1000 bp, human, alien, missing type information regulation 2 homolog 7 (S. pombe)
1155	0.9242	0.8591	0.7712	0.9317	1.0225	16	retrotransposon, 1000 bp, human, alien, missing type information regulation 2 homolog 7 (S. pombe)
1156	0.8340	0.7853	0.7171	0.9216	1.0225	16	retrotransposon, 1000 bp, human, alien, missing type information regulation 2 homolog 7 (S. pombe)
1157	0.9563	0.7853	0.7171	0.9216	1.0225	16	retrotransposon, 1000 bp, human, alien, missing type information regulation 2 homolog 7 (S. pombe)
1158	0.8253	0.7608	0.6957	0.7984	0.8143	16	Mus musculus, clone MGC-36383 IMAGE:508924, mRNA, complete cds
1159	0.9553	0.7901	0.7037	0.9032	0.9327	16	Mus musculus, clone MGC-36383 IMAGE:508924, mRNA, complete cds
1160	1.0320	0.8286	0.7437	0.9322	0.9812	16	corollin-like growth factor binding protein 2
1161	0.9159	0.8189	0.7437	0.9322	0.9812	16	corollin-like growth factor binding protein 2
1162	0.9457	0.8189	0.7437	0.9322	0.9812	16	corollin-like growth factor binding protein 2
1163	1.0278	0.8189	0.7437	0.9322	0.9812	16	corollin-like growth factor binding protein 2
1164	1.0041	0.8189	0.7437	0.9322	0.9812	16	corollin-like growth factor binding protein 2
1165	1.0041	0.8189	0.7437	0.9322	0.9812	16	corollin-like growth factor binding protein 2
1166	0.9755	0.8457	0.7552	0.9649	0.9476	16	corollin-like growth factor binding protein 2
1167	0.9118	0.8582	0.7946	0.9356	0.9356	16	corollin-like growth factor binding protein 2
1168	1.0686	0.8594	0.8360	0.9758	1.1393	16	corollin-like growth factor binding protein 2
1169	0.9471	0.8302	0.7884	0.9466	1.0455	16	corollin-like growth factor binding protein 2
1170	0.9471	0.8302	0.7884	0.9466	1.0455	16	corollin-like growth factor binding protein 2
1171	0.9471	0.8302	0.7884	0.9466	1.0455	16	corollin-like growth factor binding protein 2
1172	0.9471	0.8302	0.7884	0.9466	1.0455	16	corollin-like growth factor binding protein 2
1173	0.9471	0.8302	0.7884	0.9466	1.0455	16	corollin-like growth factor binding protein 2
1174	0.9471	0.8302	0.7884	0.9466	1.0455	16	corollin-like growth factor binding protein 2
1175	0.9471	0.8302	0.7884	0.9466	1.0455	16	corollin-like growth factor binding protein 2
1176	0.9471	0.8302	0.7884	0.9466	1.0455	16	corollin-like growth factor binding protein 2
1177	1.0189	0.5147	0.5892	0.8992	0.8150	16	corollin-like growth factor binding protein 2
1178	1.0214	0.8563	0.8755	1.0146	0.8603	16	corollin-like growth factor binding protein 2
1179	0.9818	0.8350	0.8525	0.9549	0.9412	16	corollin-like growth factor binding protein 2
1180	1.0657	0.8276	0.8304	0.9549	0.8849	16	corollin-like growth factor binding protein 2
1181	0.9447	0.8596	0.8314	1.0452	0.9370	16	corollin-like growth factor binding protein 2
1182	1.0488	0.7387	0.7588	1.0728	0.9178	16	corollin-like growth factor binding protein 2
1183	0.9530	0.7481	0.7435	1.0938	0.9276	16	corollin-like growth factor binding protein 2
1184	1.0471	0.8715	0.8655	1.0884	1.0194	16	corollin-like growth factor binding protein 2
1185	1.0434	0.8567	0.8687	1.0590	1.0021	16	corollin-like growth factor binding protein 2
1186	0.9598	0.7986	0.7870	1.0667	0.9204	16	corollin-like growth factor binding protein 2
1187	1.1232	0.7823	0.7875	1.2412	1.0434	16	corollin-like growth factor binding protein 2
1188	1.0409	0.8278	0.8049	1.0587	1.0152	16	corollin-like growth factor binding protein 2
1189	0.9439	0.8329	0.8138	0.9656	0.9398	16	corollin-like growth factor binding protein 2
1190	1.0047	0.8441	0.7723	1.0302	0.9481	16	corollin-like growth factor binding protein 2

1191	1.0120	0.8337	0.7487	1.0356	0.8979	16	hercokines 1
1192	1.0384	0.9324	0.9168	1.0256	0.9948	16	RIKEN cDNA 2310010C13 gene
1193	0.9873	0.8435	0.8001	0.9836	0.9220	16	alpha-methylacyl-CoA oxidase family A, 4
1194	1.0463	0.8703	0.8228	1.1699	1.1217	16	glycylcysteine lyase family A, 4
1195	0.8462	0.4888	0.6852	1.0029	0.9328	16	glyoxalase 2, cytosolic
1196	1.1521	0.9298	0.9929	1.3168	1.1566	16	expressed sequence A3116828
1197	0.9514	0.7955	0.8686	1.0724	1.0300	16	catenin 2
1198	1.2042	1.0528	1.0486	1.0724	1.3002	16	RIKEN cDNA 573406115 gene
1199	1.1674	0.8214	1.0436	1.3230	1.2427	16	malester receptor subfamily 2, group F, member 6
1200	0.9449	0.8214	0.8173	1.0253	0.9929	16	provisional biogenesis factor 13
1201	0.9986	0.8702	0.8721	0.9801	0.9253	16	expressed sequence AW52393
1202	0.9986	0.8072	0.8256	1.0988	1.0155	16	erythrocyte protein band 4.1-like 1
1203	1.0713	0.8327	0.8878	1.2049	1.1226	16	ESTs, weakly similar to S26689 hypothetical protein hcl - mouse (M. musculus)
1204	0.9048	0.7019	0.7891	0.9459	1.1862	16	CD59a antigen
1205	0.8098	0.5689	0.6880	0.9742	1.1281	16	tetractin (plaminogen binding protein)
1206	0.8417	0.5339	0.6417	0.8740	0.9940	16	estronin (plaminogen binding protein)
1207	0.9219	0.7310	0.8274	0.9510	1.0110	16	ESTs
1208	0.9231	0.6366	0.7259	0.9127	0.9244	16	pre B-cell leukemia transcription factor 1
1209	0.7930	0.4267	0.5527	0.6926	0.8417	16	low density lipoprotein receptor-related protein 2
1210	0.8084	0.5246	0.6091	0.7451	0.8629	16	nonconductor 1
1211	1.0270	0.7353	0.8341	0.9693	1.0117	16	nonconductor 7 superfamily member 1
1212	0.8718	0.6501	0.6501	0.8650	0.8654	16	nonconductor 7 superfamily member 1
1213	0.8370	0.6398	0.6501	0.8650	0.8654	16	Williams-Beuren syndrome chromosome region 14 homolog (human)
1214	0.9320	0.7237	0.7237	0.8925	0.8692	16	RIKEN cDNA 2610524C07 gene
1215	1.0462	0.5204	0.7444	0.8933	0.9515	16	expressed sequence A1533555
1216	0.9949	0.6933	0.7449	0.9300	1.0545	16	calpain, small subunit 1
1217	0.9002	0.5735	0.6361	0.9300	1.0651	16	expressed sequence A1838057
1218	0.7460	0.6187	0.6259	0.8153	0.9450	16	vitamin D receptor
1219	1.0014	0.7697	0.7718	0.9483	0.8373	16	RIKEN cDNA A330103N21 gene
1220	0.8994	0.6916	0.7194	0.9090	1.0921	16	PH domain containing protein in retina 1
1221	0.9126	0.7771	0.7863	0.9175	0.9422	16	insulin-like growth factor binding protein, acid labile subunit
1222	1.0124	0.7874	0.7765	0.9927	0.9253	16	Mus musculus clone IMAGE315544, mRNA, partial cds
1223	1.1773	0.9770	0.9666	1.1599	1.0544	16	RIKEN cDNA 2610039B05 gene
1224	1.0799	0.7978	0.8182	1.0755	1.2159	16	RIKEN cDNA 2610068K17 gene
1225	1.0972	0.8667	0.8667	1.1984	1.1785	16	proton-ATPase family, member B
1226	0.7216	0.4264	0.5756	0.6703	1.1788	16	RIKEN cDNA 11101G110 gene
1227	0.9077	0.6041	0.7360	0.7749	0.9598	16	phosphatase 16, cytosolic
1228	0.8997	0.6488	0.7352	0.9786	0.9786	17	phosphatase 2 (Drosophila)
1229	0.8753	0.7748	0.7542	0.7460	0.9231	17	acetyl-CoA: Coenzyme A transferase
1230	0.9602	0.6947	0.6947	0.7941	0.9231	17	expressed sequence A1524491
1231	0.9466	0.6472	0.6568	0.7941	1.0685	17	thiamine pyrophosphokinase
1232	0.7884	0.7072	0.6684	0.6223	0.8250	17	kuvenenase (L-lysine/lysine hydrolase)
1233	0.8275	0.8975	0.5174	0.5960	0.8833	18	RIKEN cDNA 061006F02 gene
1234	0.8275	0.8975	0.5174	0.5960	0.4893	18	acyl-CoA: Coenzyme A oxidase 1, palmitoyl
1235	0.9488	0.9660	0.7584	0.7499	0.6500	18	soluble carrier family 22 (organic anion transporter), member 6
1236	1.0921	1.2183	0.6037	0.6404	0.8044	18	thiodioxin 2
1237	1.0921	1.2183	0.6037	0.6404	0.7653	18	glutathione S-transferase, alpha 2 (Yc2)

1237	0.8047	1.2511	0.7664	0.6000	0.7622	18	heat shock protein, 63 kDa
1238	0.7910	1.0130	0.6032	0.6235	0.7714	18	glycerol phosphate dehydrogenase 1, mitochondrial
1239	0.6354	0.7465	0.4653	0.5398	0.5464	18	5S ribosomal protein 251 (kDa)
1240	0.8518	0.9328	0.7476	0.6555	0.7288	18	ESTs
1241	0.8175	1.1026	0.8252	0.9639	0.7661	18	X transporter protein 2
1242	0.9132	0.9692	0.7408	0.8350	0.8091	18	induced expression 3
1243	0.6794	0.9598	0.7827	0.8830	0.8372	18	cytochrome P450, subfamily IV B, polypeptide 1
1244	0.8882	1.1147	0.7188	0.7641	0.8372	18	muscle myosin heavy chain 2, adult
1245	0.8922	1.1147	0.7188	0.7641	0.8372	18	expressed sequence A6461788
1246	0.8922	1.1147	0.7188	0.7641	0.8372	18	expressed sequence A6461788
1247	0.8922	1.1147	0.7188	0.7641	0.8372	18	expressed in non-metastatic cells 2, protein (NM23B) (nucleoside diphosphate kinase)
1248	0.8922	1.1147	0.7188	0.7641	0.8372	18	hydronium mediated motility receptor (RHAMM)
1249	0.8922	1.1147	0.7188	0.7641	0.8372	18	activator of S phase kinase
1250	0.8922	1.1147	0.7188	0.7641	0.8372	18	ESTs
1251	0.8922	1.1147	0.7188	0.7641	0.8372	18	Unknown
1252	0.8922	1.1147	0.7188	0.7641	0.8372	18	RIKEN cDNA 7000381823 gene
1253	0.8922	1.1147	0.7188	0.7641	0.8372	18	RIKEN cDNA 7000381823 gene
1254	0.8922	1.1147	0.7188	0.7641	0.8372	18	RIKEN cDNA 7000381823 gene
1255	0.8922	1.1147	0.7188	0.7641	0.8372	18	cell division cycle 25 homolog A (S. cerevisiae)
1256	0.8922	1.1147	0.7188	0.7641	0.8372	18	ESTs, Weakly similar to T2M029 hypothetical protein F53G12.3 - Cuonotabilis elegans (Colegans)
1257	0.8922	1.1147	0.7188	0.7641	0.8372	18	serine (or cysteine) proteinase inhibitor, chitinase B (ovalbumin), member 2
1258	0.8922	1.1147	0.7188	0.7641	0.8372	18	ESTs
1259	0.8922	1.1147	0.7188	0.7641	0.8372	18	Mus musculus mRNA for 67 kDa polymerase-associated factor PAF67 (pat67 gene)
1260	0.8922	1.1147	0.7188	0.7641	0.8372	18	ESTs
1261	0.8922	1.1147	0.7188	0.7641	0.8372	18	retin 2, tandem duplication of Ret1
1262	0.8922	1.1147	0.7188	0.7641	0.8372	18	Mus musculus, clone MGC:18871 IMAGE:4234793, mRNA, complex cds
1263	0.8922	1.1147	0.7188	0.7641	0.8372	18	ESTs
1264	0.8922	1.1147	0.7188	0.7641	0.8372	18	inducible C/EBP binding protein 2
1265	0.8922	1.1147	0.7188	0.7641	0.8372	18	transin
1266	0.8922	1.1147	0.7188	0.7641	0.8372	18	PVA polymerase associated factor, 53 kD
1267	0.8922	1.1147	0.7188	0.7641	0.8372	18	glutathione peroxidase 2
1268	0.8922	1.1147	0.7188	0.7641	0.8372	18	enzyme 5-phosphatase dehydrogenase 2
1269	0.8922	1.1147	0.7188	0.7641	0.8372	18	uridine diphosphate kinase, structural
1270	0.8922	1.1147	0.7188	0.7641	0.8372	18	expressed sequence AB257255
1271	0.8922	1.1147	0.7188	0.7641	0.8372	18	canine palmitoyltransferase 2
1272	0.8922	1.1147	0.7188	0.7641	0.8372	18	RIKEN cDNA 25000741.19 gene
1273	0.8922	1.1147	0.7188	0.7641	0.8372	18	expressed sequence A852479
1274	0.8922	1.1147	0.7188	0.7641	0.8372	18	Mus musculus adult male Kidney cDNA, RIKEN full-length cDNA library, clone0610012C11, homogenate 1, 2-deoxyribose, full insert sequence
1275	0.8922	1.1147	0.7188	0.7641	0.8372	18	expressed sequence AB248669
1276	0.8922	1.1147	0.7188	0.7641	0.8372	18	period homolog 2 (Drosophila)
1277	0.8922	1.1147	0.7188	0.7641	0.8372	18	AMP deaminase 3
1278	0.8922	1.1147	0.7188	0.7641	0.8372	18	ESTs
1279	0.8922	1.1147	0.7188	0.7641	0.8372	18	ESTs
1280	0.8922	1.1147	0.7188	0.7641	0.8372	18	RIKEN cDNA 2700099C19 gene

1281	1.0470	1.0996	1.3180	1.0282	1.1319	22	FK506 binding protein 9
1282	0.8497	0.6632	0.8776	0.6948	0.7460	23	selenophosphate synthetase 2
1283	0.7892	0.6607	0.8061	0.6815	0.6965	23	prion protein
1284	0.9023	0.4449	0.8809	0.5662	0.5433	23	NADPH oxidase 4
1285	1.0404	0.4635	1.1677	0.7781	0.7421	23	2-hydroxyphenyl-CoA lyase
1286	0.8847	0.7504	0.9388	0.7553	0.7135	23	four and a half LIM domains 1
1287	0.9811	0.7886	0.9567	0.7790	0.7844	23	lysine acid binding protein 2
1288	1.2003	1.0812	1.2903	1.3502	1.4216	24	transcription factor 10
1289	1.2993	1.0302	1.2843	1.0675	1.0675	24	ESR1 - Wnt3a target to JF5096 (ovocellin - mouse (M. musculus))
1290	1.0760	0.8838	1.0643	1.2095	1.2461	24	retinol-binding protein 4
1291	1.0583	1.1440	1.2454	1.0365	1.3095	25	Mus musculus, Similar to RAS p21 protein activator, clone MGC:7759 IMAGE3468774, mRNA, complete cds
1292	0.7509	0.7341	0.8281	0.6906	0.8322	26	RIKEN cDNA 170012B18 gene
1293	0.7475	0.7636	0.7379	0.6815	0.7817	27	Mus musculus, Similar to angiotensin-like factor, clone MGC:5043159, mRNA, complete cds



**Table 15.** The RRR 1325 genes expression data and specific functional gene-clusters, 1325 unique genes were identified in the current microarray dataset. The gene expression is presented as up or down from normal-ischemic kidneys. Two separate groups of microarray experiments were conducted, and the results were subsequently normalized to eliminate systematic bias. The first group consisted of normal and ischemic tissues, as well as 1 and 2 days post-injury. The second group consisted of normal kidneys and 5 and 14 days post-injury. The data from days 1 and 2 were normalized by the mean of the normal-ischemic group, and the data from days 5 and 14 by the mean of the corresponding normal kidney. The genes were further clustered according to RCC vs. normal kidney; renal cell culture hypoxia responsive genes vs. normoxia; HIF regulated genes; VHL, IGF1, MYC, NF- $\kappa$ B pathway genes; purine pathway genes; gene expression following renal ischemia reperfusion and/or acute renal failure (ARF) vs. normal tissue; and gene expression in response to serum (1, 2).

Gene name	Symbol Human	Time points: Early (A); Late (B); Early & late (*) changed gene	p-value (days 1-2 vs Normal-Ischemic)
(Gus-s) beta-glucuronidase structural	GUSB	b	
(Prlr-rs1) prolactin receptor related sequence 1	PRLR	*	0.0005
(Sdcccag28) serologically defined colon cancer antigen 28	STARD10	a	0.0012
((AW146109) expressed sequence AW146109)	CD44	*	0.0018
(2610524K.04Kik; RIKEN cD 2610524K04 gene)	pp90RSK4	a	0.0013
1-acylglycerol-3-phosphate O-acyltransferase 3; expressed sequence AW493985	AGPAT3	a	0.0042
2'-5' oligoadenylate synthetase 1A	OAS1	a	0.0202
2-hydroxyphytanoyl-CoA lyase	HPCL2	b	
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1	HMGCS1	a	0.0011
3-phosphoglycerate dehydrogenase	PHGDH	a	0.0018
4-hydroxyphenylpyruvic acid dioxygenase	HPD	*	0.0005
5',3' nucleotidase, cytosolic	NTSC	b	
5-azacytidine induced gene 1	Azi1	a	0.0079
a disintegrin and metalloprotease domain 12 (meltrin alpha)	ADAM12	*	0.019
a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 1	ADAMTS1	*	0.0005
a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 2	ADAMTS2	a	0.0347
A kinase (PRKA) anchor protein 2	AKAP2	a	0.0215

acetyl-Coenzyme A acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (D18Erd240e) RIKEN cD0610011L04 gene	ACAA2	*	0.0006
acetyl-Coenzyme A dehydrogenase, medium chain	ACADM	a	0.0005
acetyl-Coenzyme A transporter	ACATN	a	0.0064
acidic ribosomal phosphoprotein PO	RPLP0	a	0.0006
aconitase 1	ACO1	b	
actin related protein 2/3 complex, subunit 3 (21 kDa)	ARPC3	a	0.0023
actin, alpha 1, skeletal muscle	ACTA1	b	
actin, alpha 2, smooth muscle, aorta	ACTA2	*	0.0005
actin, beta, cytoplasmic	ACTB	*	0.0005
actin, gamma 2, smooth muscle, enteric	ACTG2	*	0.013
actin-like	ACTG1	*	0.0005
activator of S phase kinase	ASK	a	0.0283
activity-dependent neuroprotective protein	ADNP	b	
acyl-Coenzyme A dehydrogenase, short/branched chain	ACADSB	*	0.0245
acyl-Coenzyme A dehydrogenase, very long chain	ACADVL	b	
acyl-Coenzyme A oxidase 1, palmitoyl	ACOX1	b	
adaptor-related protein complex AP-3, sigma 1 subunit	AP3S1	a	0.0109
adducin 3 (gamma)	ADD3	b	
adenine phosphoribosyl transferase	APRT	b	
adenylate cyclase 4	ADCY4	a	0.0472
adenylate kinase 4	Ak4	*	0.0008
adenylosuccinate synthetase 2, non muscle	ADSS	(a+b)=*	0.004
adenylyl cyclase-associated CAP protein homolog 1 (S. cerevisiae, S. pombe)	CAP	a	0.0127
ADP-ribosylation factor 1	ARF1	a	0.0012
ADP-ribosyltransferase (D+)	ADPRTL2	a	0.003
AE binding protein 1	AEBP1	b	
ajuba	JUB	b	
alcohol dehydrogenase 4 (class II), pi polypeptide	ADH4	b	
aldehyde dehydrogenase family 1, subfamily A2	ALDH1A2	b	
aldo-keto reductase family 1, member B8 ((Fgfip) fibroblast growth factor regulated protein)	AKR1B10	*	0.0016
aldo-keto reductase family 1, member C18 ; expressed sequence AW146047	Akr1c18	a	0.0025
alkaline phosphatase 2, liver	ALPL	a	0.0096
ALL1-fused gene from chromosome 1q	AF1Q	a	0.0049
alpha-methylacyl-CoA racemase	AMACR	a	0.0472
amelogenin	AMELX	b	
amiloride binding protein 1 (amine oxidase, copper-containing)	ABP1	*	0.005
amine N-sulfotransferase	Sultn	a	0.0472
aminoadipate-semialdehyde synthase/ (Lorsdh) lysine oxoglutarate reductase, saccharopine dehydrogenase	AASS	*	0.0008
AMP deaminase 3	AMPD3	b	
annexin A1	ANXA1	b	
annexin A2	ANXA2	*	0.0005
annexin A3	ANXA3	b	
annexin A4	ANXA4	b	
annexin A5	ANXA5	*	0.0005
annexin A6	ANXA6	*	0.0005

anterior gradient 2 ( <i>Xenopus laevis</i> )	AGR2	a	0.0044
apolipoprotein B editing complex 1	APOBEC1	b	
apolipoprotein E	APOE	b	
apoptosis inhibitory protein 5	API5	b	
apurinic/apyrimidinic endonuclease	APEX1	a	0.0005
aquaporin 2	AQP2	a	0.0027
arachidate 12-lipoxygenase, pseudogene 2	ALOX12P2	b	
arachidate 5-lipoxygenase activating protein	ALOX5AP	a	0.0135
arginine-rich, mutated in early stage tumors	ARMET	a	0.0013
argase type II	ARG2	b	
Arpc2	ARPC2	*	0.0005
ATP synthase, H <sup>+</sup> transporting mitochondrial F1 complex, beta subunit	ATP5B	a	0.0081
ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, alpha subunit, isoform 1	ATP5A1	a	0.0035
ATPase, H <sup>+</sup> transporting, beta 1 polypeptide	ATP1B1	b	
ATPase, H <sup>+</sup> transporting, lysosomal (vacuolar proton pump), alpha 70 kDa, isoform 1	ATP6V1A1	a	0.0269
ATPase, H <sup>+</sup> transporting, V1 subunit F; RIKEN cD1110004G16 gene	ATP6V1F	a	0.0028
ATPase, H <sup>+</sup> /K <sup>+</sup> transporting, alpha polypeptide	ATP4A	a	0.0231
ATP-binding cassette, sub-family A (ABC1), member 7	ABCA7	b	
ATP-binding cassette, sub-family D (ALD), member 3	ABCD3	*	0.0193
AU R binding protein/enoyl-coenzyme A hydratase	AUH	*	0.0012
avian reticuloendotheliosis viral (v-rel) oncogene related B	RELB	b	
AXL receptor tyrosine kinase	AXL	*	0.0005
baculoviral IAP repeat-containing 1a	BIRC1	*	0.0017
baculoviral IAP repeat-containing 2	BIRC3	b	
baculoviral IAP repeat-containing 3	BIRC3	b	
B-box and SPRY domain containing	BSPRY	b	
B-cell leukemia/lymphoma 2 related protein A1b	BCL2A1	*	0.0034
BCL2-antagonist/killer 1	BAK1	b	
Bcl-2-related ovarian killer protein	BOK	b	
benzodiazepine receptor, peripheral	BZRP	b	
beta-2 microglobulin	B2M	b	
betaine-homocysteine methyltransferase	BHMT	a	0.0005
biglycan	BGN	*	0.0219
bisphosphate 3'-nucleotidase 1	BPNT1	b	
Blu protein	ZMYND10	a	0.0042
bone marrow stromal cell antigen 1	BST1	*	0.03
bone morphogenetic protein receptor, type 1A	BMPR1A	b	
brain protein 44-like	BRP44I	a	0.0005
branched chain aminotransferase 2, mitochondrial	BCAT2	a	0.0005
branched chain ketoacid dehydrogenase E1, alpha polypeptide	BCKDHA	*	0.0005
breakpoint cluster region protein 1	BANF1	a	0.0005
BRG1/brm-associated factor 53A	BAF53A	*	0.0482
Bromodomain and PHD finger containing, 3	Brp3	a	0.0115
cadherin 3	CDH3	*	0.0041
calbindin-28K	CALB1	*	0.0005
calbindin-D9K	CALB3	a	0.0086

calcium channel, voltage-dependent, beta 3 subunit	CACNB3	b	
calpain 2	CAPN2	b	
calpain, small subunit 1	CAPNS1	a	0.0013
calponin 2	CNN2	*	0.0018
calreticulin	CALR	a	0.0238
calsyntenin 1	CLSTN1	a	0.0068
capping protein beta 1	CAPZB	*	0.0043
carbonic anhydrase 5a, mitochondrial	CA5A	a	0.0478
carboxylesterase 3	CBS3	*	0.0031
carboxypeptidase E	CPE	b	
carboxypeptidase X 1 (M14 family) / metallo-carboxypeptidase 1	CPXM	b	
cardiac responsive adriamycin protein	CARP	a	0.0197
carmitine palmitoyltransferase 1, liver	CPT1A	*	0.004
carmitine palmitoyltransferase 1, muscle	CPT1B	a	0.0179
carmitine palmitoyltransferase 2	CPT2	a	0.0005
cartilage oligomeric matrix protein	COMP	a	0.047
casein kase 1, epsilon	CSNK1E	b	
caspase 1	CASP1	a	0.0047
caspase 3, apoptosis related cysteine protease	CASP3	b	
caspase 8	CASP8	a	0.0215
cathepsin D	CTSD	a	0.0005
cathepsin L	CTSL	a	0.0157
cathepsin S	CTSS	*	0.0072
cathepsin Z	CTSZ	a	0.0285
Cbp/p300-interacting transactivator with Glu/Asp-rich carboxy-terminal domain 1	CITED1	b	
CCCTC-binding factor	CTCF	a	0.005
CD24a antigen	CD24	*	0.0218
CD2-associated protein	CD2AP	(a+b)=*	0.005
CD38 antigen	CD38	a	0.0043
CD48 antigen	CD48	b	
CD52 antigen	CDW52	(b+b)=b	
CD53 antigen	CD53	*	0.0096
CD59a antigen	CD59	a	0.0013
CD68 antigen	CD68	*	0.0005
CD72 antigen	CD72	*	0.0018
CDC16 (cell division cycle 16 homolog (S. cerevisiae))	CDC16	a	0.0279
CDC28 protein kase 1	CKS1B	a	0.0484
CDK2 (cyclin-dependent kase 2)-associated protein 1	CDK2AP1	a	0.0006
CEA-related cell adhesion molecule 1	CEACAM1	*	0.0135
CEA-related cell adhesion molecule 2	Ceacam2	*	0.0015
cell death-inducing D fragmentation factor, alpha subunit-like effector B	CIDEB	a	0.0031
cell division cycle 2 homolog A (S. pombe)	CDC2	a	0.0075
cell division cycle 25 homolog A (S. cerevisiae)	CDC25A	a	0.0472
cell division cycle 42 homolog (S. cerevisiae)	CDC42	*	0.0052
cellular nucleic acid binding protein	ZNF9	a	0.0012
centrin 2	CETN2	a	0.0091
centrin 3	CETN3	b	
ceroid-lipofuscinosis, neuro 2	CLN2	a	0.0041

chaperonin subunit 3 (gamma)	CCT3	a	0.001
chemokine (C-C) receptor 2	CCR2	*	0.0215
chemokine (C-C) receptor 5	CCR5	a	0.0046
chemokine orphan receptor 1	RDC1	b	
chitinase 3-like 3	CHIA	a	0.03
chloride channel calcium activated 1	CLCA1	b	
chloride channel, nucleotide-sensitive, 1A	CLNS1A	b	
chloride intracellular channel 1	CLIC1	*	0.0005
chloride intracellular channel 4 (mitochondrial)	CLIC4	*	0.0186
cholinergic receptor, nicotinic, beta polypeptide 1 (muscle)	CHRN1	b	
citrate lyase beta like	CLYBL	a	0.0021
clathrin, light polypeptide (Lca)	CLTA	a	0.0029
claudin 1	CLDN1	*	0.0005
claudin 4	CLDN4	*	0.0012
claudin 7	CLDN7	*	0.0005
cleavage and polyadenylation specific factor 5, 25 kD subunit	CPSF5	b	
clusterin	CLU	a	0.0005
coagulation factor II (thrombin) receptor-like 1	F2RL1	*	0.0005
coagulation factor III	F3	*	0.0005
coagulation factor XIII, beta subunit	F13B	*	0.0005
cofilin 1, non-muscle	CFL1	a	0.0005
cold shock domain protein A	CSDA	*	0.0005
colony stimulating factor 1 (macrophage)	CSF1	a	0.0011
complement component 1, q subcomponent, alpha polypeptide	C1QA	*	0.0096
complement component 1, q subcomponent, beta polypeptide	C1QB	b	
complement component 1, q subcomponent, c polypeptide	C1QG	b	
complement component 3	C3	*	0.0013
complement component factor i	IF	a	0.004
complement factor H related protein 3A4/5G4	HF1	(b+b)=b	
connective tissue growth factor	CTGF	b	
constitutive photomorphogenic protein 1 (Arabidopsis)	COP1	b	
coproporphyrinogen oxidase	CPO	b	
cord-bleu ; ESTs, Moderately similar to T00381 KIAA0633 protein (H.sapiens)	COBL	a	0.0185
core promoter element binding protein	COPEB	(*)+*=*	0.0052; 0.0009
cornichon homolog (Drosophila)	CNIH	a	0.03
coronin, actin binding protein 1B	CORO1B	*	0.0086
craniofacial development protein 1	CFDP1	*	0.0005
creatine kinase, brain	CKB	a	0.0099
cryptochrome 2 (photolyase-like)	CRY2	a	0.0339
crystallin, alpha B	CRYAB	a	0.0183
crystallin, lambda 1	CRYL1	*	0.0075
crystallin, mu	CRYM	*	0.0008
cyclin E1	CCNE1	a	0.0146
cyclin-dependent kinase 4	CDK4	a	0.0006
cyclin-dependent kinase inhibitor 1A (P21)	CDKN1A	a	0.0005
cystatin B	CSTB	*	0.0005
cystatin C	CST3	b	
cysteine rich protein 61	CYR61	*	0.0014

cytidine 5'-triphosphate synthase	CIPS	*	0.0006
cytidine 5'-triphosphate synthase 2	CIPS2	b	
cytochrome c oxidase, subunit VIc	COX6C	a	0.0052
cytochrome c oxidase, subunit VIIa 1	COX7A1	a	0.0099
cytochrome c oxidase, subunit VIIa 3	COX7A3	a	0.0497
cytochrome c oxidase, subunit VIIa	COX8	b	
cytochrome P450, 2a4	CYP2A13	(*)=*	0.0008; 0.0186
cytochrome P450, 2d9	CYP2D6	(a+b)=*	0.0005
cytochrome P450, 2e1, ethanol inducible	CYP2E1	a	0.0082
cytochrome P450, 2j5	CYP2J2	*	0.005
cytochrome P450, family 4, subfamily v, polypeptide 3 / expressed sequence AW111961	Cyp4v3	b	
cytochrome P450, subfamily IV B, polypeptide 1	CYP4B1	b	
cytokine inducible SH2-containing protein 3	SOCS3	*	0.0005
D methyltransferase (cytosine-5) 1	DNMT1	a	0.0015
D methyltransferase 3B	DNMT3B	a	0.0009
D primase, p49 subunit	PRIM1	a	0.0009
D segment, Chr 12, ERATO Doi 604, expressed	TSSC1	b	
D segment, Chr 17, ERATO Doi 441, expressed	D17Erd441e	*	0.0072
D segment, Chr 17, human D6S56B 2	LSM2	a	0.0045
D segment, Chr 18, Wayne State University 181, expressed	ALDH7A1	*	0.0135
D segment, Chr 8, Brigham & Women's Genetics 1320 expressed	D8Bwg1320e	a	0.0086
damage specific D binding protein 1 (127 kDa)	DDB1	a	0.0014
D-amino acid oxidase	DAO	b	
D-dopachrome tautomerase	DDT	a	0.0008
DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 50 / nucleolar protein GU2	DDX50	b	
decorin	DCN	b	
deiodinase, iodothyronine, type 1	DIO1	*	0.0005
deltex 1 homolog (Drosophila)	DTX1	a	0.0086
deoxyribonuclease I	DNASE1	*	0.0005
diaphorase 1 (DH)	DIA1	*	0.0023
dihydropyrimidase	DPYS	*	0.0021
dihydropyrimidase-like 3	DPYSL3	a	0.0218
dimethylarginine dimethylaminohydrolase 2	DDAH2	b	
dipeptidase 1 (rel)	DPEP1	*	0.0006
DJ (Hsp40) homolog, subfamily A, member 1	DNAJA1	a	0.0005
DJ (Hsp40) homolog, subfamily B, member 12	Djb12	a	0.0035
DJ (Hsp40) homolog, subfamily C, member 5	DNAJC5	b	
dolichyl-di-phosphooligosaccharide-protein glycotransferase	DDOST	a	0.0013
dopa decarboxylase	DDC	a	0.0047
double cortin and calcium/calmodulin-dependent protein kinase-like 1	DCAMK1L	a	0.0042
downstream of tyrosine kinase 1	DOK1	b	
DPH oxidase 4	NOX4	b	
E26 avian leukemia oncogene 2, 3' domain	ETS2	a	0.0012
E74-like factor 3	ELF3	*	0.0312
E74-like factor 4 (ets domain transcription factor)	ELF4	*	0.0023

early development regulator 2 (homolog of polyhomeotic 2)	EDR2	b	
ectonucleoside triphosphate diphosphohydrolase 5	ENTPD5	a	0.0313
ectonucleotide pyrophosphatase/phosphodiesterase 2	ENPP2	*	0.0005
EGF-like module containing, mucin-like, hormone receptor-like sequence 1	EMR1	b	
EGL nine homolog 1 ( <i>C. elegans</i> )	EGLN1	a	0.0008
elafin-like protein 1	SWAM1	a	0.0005
elastase 1, pancreatic	ELA1	a	0.0005
elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 1	ELOVL1	*	0.0012
endonuclease G	ENDOG	a	0.0014
endoplasmic reticulum protein 29	C12orf8	b	
endothelin 1	EDN1	*	0.0057
enhancer of zeste homolog 2 ( <i>Drosophila</i> )	EZH2	a	0.0018
enoyl Coenzyme A hydratase, short chain, 1, mitochondrial	ECHS1	a	0.0005
epidermal growth factor	EGF	*	0.0005
epidermal growth factor-containing fibulin-like extracellular matrix protein 1	EFEMP1	b	
epidermal growth factor-containing fibulin-like extracellular matrix protein 2	EFEMP2	*	0.0006
epithelial membrane protein 3	EMP3	*	0.0009
erythrocyte protein band 4.1 / <i>Mus musculus</i> adult male tongue cD, RIKEN full-length enriched library, clone:2310065B16:erythrocyte protein band 4.1, full insert sequence	EPB41	b	
erythrocyte protein band 4.1-like 1	EPB41L1	a	0.0009
erythroid differentiation regulator	edr	a	0.0424
EST AI181838	MGC2555	a	0.0005
estrogen related receptor, alpha	ESRRA	a	0.0023
ESTs		*	0.0041
ESTs		*	0.006
ESTs		a	0.0022
ESTs		a	0.0012
ESTs		a	0.0125
ESTs		a	0.0014
ESTs		a	0.0381
ESTs	Rin3	a	0.0012
ESTs		a	0.0006
ESTs		a	0.0026
ESTs		a	0.0006
ESTs		a	0.0005
ESTs		a	0.0048
ESTs		a	0.0015
ESTs		a	0.0217
ESTs		a	0.03
ESTs		a	0.0072
ESTs		a	0.018
ESTs		a	0.0005
ESTs		a	0.0118
ESTs		a	0.0067
ESTs		a	0.0307
ESTs		a	0.0023

ESTs		a	0.0018
ESTs		a	0.0381
ESTs		a	0.0013
ESTs		a	0.0268
ESTs		a	0.0033
ESTs		b	
ESTs		b	
ESTs		b	
ESTs		b	
ESTs	FLJ22184	b	
ESTs		b	
ESTs	9130203F04Rik	b	
ESTs		b	
ESTs		b	
ESTs		b	
ESTs	1110069O07Rik	b	
ESTs	FLJ23447	b	
ESTs		b	
ESTs		b	
ESTs -pending	PCSK9	a	0.0031
ESTs, Highly similar to prefoldin 4 (Homo sapiens) (H.sapiens)	PFDN4	a	0.006
ESTs, Highly similar to organic cation transporter-like protein 2 (M.musculus)		a	0.0015
ESTs, Highly similar to T00268 hypothetical protein KIAA0597 (H.sapiens)	KIAA0597	a	0.0005
ESTs, Moderately similar to SEC7 homolog (Homo sapiens) (H.sapiens)		b	
ESTs, Moderately similar to S12207 hypothetical protein (M.musculus)		*	0.0005
ESTs, Moderately similar to T08673 hypothetical protein DKFZp564C0222.1 (H.sapiens)	KIAA0977	*	0.0343
ESTs, Moderately similar to T46312 hypothetical protein DKFZp434J1111.1 (H.sapiens)		b	
ESTs, Weakly similar to brain-specific angiogenesis inhibitor 1-associated protein 2 (Mus musculus) (M.musculus)		a	0.0219
ESTs, Weakly similar to limb expression 1 homolog (chicken) (Mus musculus) (M.musculus)		a	0.0118
ESTs, Weakly similar to simple repeat sequence-containing transcript (Mus musculus) (M.musculus)		b	
ESTs, Weakly similar to 2022314A granule cell marker protein (M.musculus)		b	
ESTs, Weakly similar to ADT1 MOUSE ADP,ATP CARRIER PROTEIN, HEART/SKELETAL MUSCLE ISOFORM T1 (M.musculus)		a	0.0018
ESTs, Weakly similar to ADT1 MOUSE ADP,ATP CARRIER PROTEIN, HEART/SKELETAL MUSCLE ISOFORM T1 (M.musculus)	SLC25A16	a	0.0133
ESTs, Weakly similar to AF182426 1 arylacetamide deacetylase (R.norvegicus)		*	0.0472



ESTs, Weakly similar to B Chain B, Crystal Structure Of Murine Soluble Epoxide Hydrolase Complexed With Cdu Inhibitor ( <i>M.musculus</i> )		b	
ESTs, Weakly similar to DRR1 ( <i>H.sapiens</i> )		*	0.0017
ESTs, Weakly similar to JC7182 +-dependent vitamin C ( <i>H.sapiens</i> )	SLC23A3	a	0.0472
ESTs, Weakly similar to JE0096 myocilin - mouse ( <i>M.musculus</i> )		b	
ESTs, Weakly similar to MAJOR URINARY PROTEIN 4 PRECURSOR ( <i>M.musculus</i> )		b	
ESTs, Weakly similar to S26689 hypothetical protein hc1 - mouse ( <i>M.musculus</i> )		a	0.0135
ESTs, Weakly similar to S65210 hypothetical protein YPL191c - yeast ( <i>Saccharomyces cerevisiae</i> ) ( <i>S.cerevisiae</i> )		a	0.0049
ESTs, Weakly similar to T29029 hypothetical protein F53G12.5 - <i>Caenorhabditis elegans</i> ( <i>C.elegans</i> )	4931439A04Rik	a	0.0006
ESTs, Weakly similar to TS13 MOUSE TESTIS-SPECIFIC PROTEIN PBS13 ( <i>M.musculus</i> )	MGC39016	b	
ESTs, Weakly similar to TYROSINE-PROTEIN KISE JAK3 ( <i>M.musculus</i> )		*	0.0147
ESTs, Weakly similar to TYROSINE-PROTEIN KISE JAK3 ( <i>M.musculus</i> )		a	0.0086
ESTs, Weakly similar to TYROSINE-PROTEIN KISE JAK3 ( <i>M.musculus</i> )	C1QR1	a	0.0185
ESTs, Weakly similar to YAE6_YEAST HYPOTHETICAL 13.4 KD PROTEIN IN ACS1-GCV3 INTERGENIC REGION ( <i>S.cerevisiae</i> )		a	0.0175
ESTs, Weakly similar to YMP2_CAEEL HYPOTHETICAL 30.3 KD PROTEIN B0361.2 IN CHROMOSOME III ( <i>C.elegans</i> )	3230401L03Rik	*	0.0005
eukaryotic translation initiation factor 2A	eIF2a	b	
eukaryotic translation initiation factor 3	EIF3S10	a	0.0016
eukaryotic translation initiation factor 3, subunit 4 (delta, 44 kDa)	EIF3S4	a	0.0009
eukaryotic translation initiation factor 4, gamma 2	EIF4G2	a	0.0424
eukaryotic translation initiation factor 4A1	EIF4A1	*	0.0135
eukaryotic translation initiation factor 4A2	EIF4A2	a	0.0014
eukaryotic translation initiation factor 4E binding protein 1	EIF4EBP1	*	0.0078
eukaryotic translation initiation factor 5A	EIF5A	a	0.0005
E-vasodilator stimulated phosphoprotein	EVL	b	
exportin 1, CRM1 homolog (yeast)	XPO1	a	0.0008
expressed in non-metastatic cells 2, protein (NM23B) (nucleoside diphosphate kase)	NME2	a	0.0096
expressed sequence AA408783	SPEC2	b	
expressed sequence AA589392	AA589392	a	0.0011
expressed sequence AA672638	AA672638	a	0.0201
expressed sequence AI117581	AI117581	a	0.0424
expressed sequence AI118577	ZNF14	(a+b)=*	0.0005
expressed sequence AI132189	AI132189	a	0.0068
expressed sequence AI132321	AI132321	*	0.0086
expressed sequence AI159688	AI159688	*	0.0006
expressed sequence AI182282	SLC9A8	a	0.0005
expressed sequence AI182284	AI182284	*	0.0012

expressed sequence AI194696	HFL1	b	
expressed sequence AI265322	AI265322	a	0.0016
expressed sequence AI314027	GLS	b	
expressed sequence AI315037	AI315037	a	0.0117
expressed sequence AI316828	FLJ20618	b	
expressed sequence AI413331	AI413331	b	
expressed sequence AI447451	AI447451	b	
expressed sequence AI448003	AI448003	b	
expressed sequence AI449309	AI449309	b	
expressed sequence AI450991	KIAA0729	a	0.0285
expressed sequence AI461788	AI461788	a	0.0026
expressed sequence AI465301	AI465301	a	0.0021
expressed sequence AI480660	AI480660	a	0.0012
expressed sequence AI504062	AI504062	*	0.033
expressed sequence AI507121	AI507121	a	0.0005
expressed sequence AI528491	AI528491	a	0.0208
expressed sequence AI553555	AI553555	a	0.0018
expressed sequence AI558103	LRRN1	a	0.025
expressed sequence AI586180	AI586180	*	0.0231
expressed sequence AI593249	AI593249	*	0.0005
expressed sequence AI593524	DKFZp586A011.1	b	
expressed sequence AI604920	KIAA0297 KIAA0329	b	
expressed sequence AI607846	AIF1	*	0.0116
expressed sequence AI646725	MDS028	b	
expressed sequence AI661919	AI661919	b	
expressed sequence AI835705	AI835705	a	0.0012
expressed sequence AI836219	AI836219	a	0.0165
expressed sequence AI838057	AI838057	a	0.0013
expressed sequence AI843960	RBPSUH	b	
expressed sequence AI844685	MGC15429	a	0.0014
expressed sequence AI844876	AI844876	b	
expressed sequence AI848669	AI848669	a	0.0497
expressed sequence AI852479	CDKL3	a	0.0005
expressed sequence AI875199	AI875199	a	0.0041
expressed sequence AI875557	AI875557	a	0.0009
expressed sequence AI957255	KIAA0564	a	0.0012
expressed sequence AI987692	AI987692	b	
expressed sequence AL022757	5730453116Rik	a	0.0005
expressed sequence AU015645	AU015645	*	0.0006
expressed sequence AU018056	AU018056	a	0.0068
expressed sequence AU019833	C1orf24	b	
expressed sequence AU042434	AU042434	b	
expressed sequence AV046379	AV046379	*	0.0012
expressed sequence AW045860	AW045860	b	
expressed sequence AW047581	AW047581	b	
expressed sequence AW124722	AW124722	a	0.0316
expressed sequence AW261723	SLC17A3	*	0.0025
expressed sequence AW413625	FLJ22794	a	0.0497

expressed sequence AW488255	EFNB1	a	0.0477
expressed sequence AW493404	AW493404	b	
expressed sequence AW541137	NUP107	b	
expressed sequence AW552393	AW552393	a	0.0239
expressed sequence AW743884	AW743884	b	
expressed sequence BB120430	BB120430	a	0.0099
expressed sequence C79732	C79732	a	0.0005
expressed sequence C80913	C80913	b	
expressed sequence C81457	FLJ21022	b	
expressed sequence C85317	C85317	b	
expressed sequence C85457	C85457	a	0.0483
expressed sequence C86169	C86169	a	0.0046
expressed sequence C86302	C86302	a	0.0013
expressed sequence C87222	C87222	*	0.0012
expressed sequence R75232	R75232	a	0.001
Fas apoptotic inhibitory molecule	FAIM	b	
fatty acid synthase	FASN	a	0.0023
f-box only protein 3	FBXO3	a	0.0119
Fc receptor, IgE, high affinity I, gamma polypeptide	FCER1G	*	0.0023
Fc receptor, IgG, low affinity III	FCGR3A	*	0.0025
feline sarcoma oncogene	FES	a	0.01
fibrillarin	FBL	a	0.0068
fibrillin 1	FBN1	*	0.0009
fibulin 5	FBLN5	a	0.002
FK506 binding protein 10 (65 kDa)	FKBP10	a	0.0005
FK506 binding protein 12-rapamycin associated protein 1	FRAP1	*	0.0022
FK506 binding protein 1a (12 kDa)	FKBP1A	a	0.0005
FK506 binding protein 5 (51 kDa)	FKBP5	b	
FK506 binding protein 9	FKBP9	a	0.0347
flap structure specific endonuclease 1	FEN1	a	0.0398
flavin containing monooxygenase 1	FMO1	a	0.0159
flotillin 1	FLOT1	a	0.0005
flotillin 2	FLOT2	a	0.0103
folate receptor 1 (adult)	FOLR1	*	0.0008
forkhead box M1	FOXM1	a	0.0023
four and a half LIM domains 1	FHL1	b	
fragile histidine triad gene	FHIT	a	0.0026
fumarylacetoacetate hydrolase	FAH	*	0.0008
FXYD domain-containing ion transport regulator 2	FXYD2	b	
FXYD domain-containing ion transport regulator 5	FXYD5	*	0.0005
G protein-coupled receptor kise 7	MKNK2	a	0.001
G1 to phase transition 1	GSPT1	a	0.0331
gamma-glutamyl hydrolase	GGH	b	
gamma-glutamyl transpeptidase	GGT1	*	0.0047
ganglioside-induced differentiation-associated-protein 3	MRPS33	b	
gap junction membrane channel protein beta 2	GJB2	b	
glucose regulated protein, 58 kDa	GRP58	a	0.0006
glucose-6-phosphatase, catalytic	G6PC	*	0.0046

glucose-6-phosphatase, transport protein 1	G6PT1	a	0.0005
glutamine synthetase	GLUL	(*+*)=*	0.0179
glutaryl-Coenzyme A dehydrogenase	GCDH	*	0.0034
glutathione peroxidase 1	GPX1	a	0.0177
glutathione S-transferase, alpha 2 (Yc2)	GSTA2	b	
glutathione S-transferase, alpha 4	GSTA4	b	
glutathione S-transferase, mu 6	GSTM1	a	0.0096
glutathione S-transferase, pi 1	GSTP1	a	0.0124
glutathione S-transferase, theta 2	GSTT2	a	0.0013
glutathione transferase zeta 1 (maleylacetoacetate isomerase)	GSTZ1	a	0.0009
glycerol kase	GK	*	0.0287
glycerol phosphate dehydrogenase 1, mitochondrial	GPD2	b	
glycerol-3-phosphate acyltransferase, mitochondrial	GPAT	*	0.0005
glycine amidinotransferase (L-arginine:glycine amidinotransferase)	GATM	*	0.0005
glycine N-methyltransferase	GNMT	a	0.0422
glycoprotein 49 A	Gp49a	*	0.0006
glycoprotein 49 B	Gp49b	*	0.0005
glypican 3	GPC3	b	
golgi autoantigen, golgin subfamily a, 4	GOLGA4	a	0.0009
golgi reassembly stacking protein 2	GORASP2	*	0.005
GPI-anchored membrane protein 1	M11S1	a	0.0115
granulin	GRN	a	0.0227
G-rich RNA sequence binding factor 1 (D5Wsu31c) D segment, Chr 5, Wayne State University 31, expressed	GRSF1	b	
group specific component	GC	a	0.0466
growth arrest and D-damage-inducible 45 alpha	GADD45A	*	0.0008
growth arrest and D-damage-inducible 45 gamma	GADD45G	b	
growth arrest specific 2	GAS2	*	0.0008
growth differentiation factor 15	PLAB	*	0.0047
growth differentiation factor 8	GDF8	b	
growth factor receptor bound protein 7	GRB7	a	0.0013
guanine nucleotide binding protein (G protein), gamma 2 subunit	GNG2	b	
guanine nucleotide binding protein (G protein), gamma 5 subunit	GNG5	*	0.0005
guanine nucleotide binding protein, alpha inhibiting 2	GNAI2	*	0.0067
guanine nucleotide binding protein, beta 2, related sequence 1	GNB2L1	*	0.0005
guanosine diphosphate (GDP) dissociation inhibitor 3	GDI-3	a	0.0312
guanosine monophosphate reductase	GMFR	*	0.0086
guanylate nucleotide binding protein 2	GBP2	b	
H2A histone family, member Z	H2AFZ	*	0.0068
H2B histone family, member S	H2BFS	a	0.0005
Harvey rat sarcoma oncogene, subgroup R	RRAS	a	0.0006
heat shock 70 kDa protein 4	HSPA4	(a+a)=a	0.0047; 0.001
heat shock protein 1 (chaperonin) / heat shock protein, 60 kDa	HSPD1	b	
heat shock protein, 105 kDa	HSPH1	b	
heat shock protein, 86 kDa 1	HSPCA	a	0.0013

hecat-responsive protein 12	UK114	a	0.0005
hematological and neurological expressed sequence 1	HN1	a	0.0008
heme oxygenase (decycling) 1	HMOX1	a	0.0393
hemochromatosis	HFE	b	
hemopoietic cell phosphatase	PTPN6	*	0.0005
heparan sulfate 2-O-sulfotransferase 1	HS2ST1	a	0.0047
heparin binding epidermal growth factor-like growth factor	DTR	a	0.019
hepatic nuclear factor 4	HNF4A	b	
hepatoma-derived growth factor	HDGF	a	0.0377
hepsin	HPN	*	0.0018
heterogeneous nuclear ribonucleoprotein A1	HNRP1	*	0.0005
hexokinase 1	HK1	a	0.0381
high mobility group AT-hook 1	HMGA1	a	0.0005
high mobility group box 3	HMGB3	*	0.0012
high mobility group nucleosomal binding domain 2	HMG2	*	0.0014
histidyl tR synthetase	HIARS	a	0.0146
histocompatibility 2, class II antigen A, alpha	HLA-DQA1	b	
histocompatibility 2, class II antigen E beta	H2-Eb1	b	
histocompatibility 2, class II, locus DMA	HLA-DMA	b	
Histocompatibility 2, D region locus 1	H2-D1	*	0.0012
histocompatibility 2, Q region locus 7	H2-Q7	b	
histone 2, H2aa1 (Hist2) histone gene complex 2	HIST2H2AA	b	
histone deacetylase 1	HDAC1	b	
homeo box B7	HOXB7	a	0.025
homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	HERPUD1	*	0.0092
Hoxc8	MCM5	a	0.0005
Hprt	HPRT1	a	0.001
hyaluron mediated motility receptor (RHAMM)	HMMR	a	0.0171
hyaluronic acid binding protein 2	HABP2	b	
hydroxysteroid 17-beta dehydrogenase 7	HSD17B7	b	
hydroxysteroid dehydrogenase-1, delta<5>-3-beta	HSD3B2	a	0.0119
hydroxysteroid dehydrogenase-3, delta<5>-3-beta	Hsd3b3	a	0.0018
hypothetical protein, I54	X61497	*	0.0005
hypothetical protein, MGC:6957	MGC6957	b	
hypothetical protein, MNCb-5210	COBRA1	b	
Ia-associated invariant chain	CD74	b	
immunoglobulin superfamily, member 8	IGSF8	a	0.0338
importin 11 (RIKEN cDNA 2510001A17 gene)	IPO11	a	0.0056
inhibin beta-B	INHBB	a	0.0005
inhibitor of D binding 2	ID2	b	
inosine 5'-phosphate dehydrogenase 2	IMPDH2	a	0.0005
inositol polyphosphate-5-phosphatase, 75 kDa	INPP5B	*	0.0005
insulin-like growth factor binding protein 1	IGFBP1	a	0.0005
insulin-like growth factor binding protein 3	IGFBP3	a	0.0005
insulin-like growth factor binding protein 4	IGFBP4	a	0.0005
insulin-like growth factor binding protein, acid labile subunit	IGFALS	a	0.0013

integrin alpha 6	ITGA6	b	
integrin alpha M	ITGAM	a	0.0224
integrin beta 1 (fibronectin receptor beta)	ITGB1	b	
integrin-associated protein	CD47	b	
intercellular adhesion molecule	ICAM1	*	0.0006
interferon activated gene 204	IFi204	(b+b)-b	
interferon gamma receptor	IFNGR1	b	
interferon inducible protein 1	IFI1	a	0.0005
interferon-induced protein with tetratricopeptide repeats 3	IFIT3	a	0.0006
integral membrane protein 1	ITM1	a	0.0047
interleukin 1 beta	IL1B	a	0.0023
interleukin 1 receptor, type I	IL1R1	a	0.0021
interleukin 11 receptor, alpha chain 1	IL11RA	a	0.0043
isocitrate dehydrogenase 2 (DP+), mitochondrial	IDH2	*	0.0023
isovaleryl coenzyme A dehydrogenase	IVD	(*+a)-*	0.0009; 0.0005
J domain protein 1	JDP1	*	0.0021
junction plakoglobin	JUP	a	0.0008
kallikrein 26	KLK26	*	0.0005
kallikrein 6	KLK1/6	*	0.0417
karyopherin (importin) alpha 2	KPNA2	a	0.0005
karyopherin (importin) beta 3	KPNB3	a	0.0068
keratin complex 1, acidic, gene 19	KRT19	b	
keratin complex 2, basic, gene 8	KRT8	*	0.0005
ketohehexokise	KHK	*	0.0005
kidney-derived aspartic protease-like protein	NAP1	*	0.005
kinectin 1	KTN1	b	
kinesin family member 1B (expressed sequence AI448212)	KIF1B	a	0.0159
kinesin family member 21A	KIF21A	a	0.0031
kise insert domain protein receptor	KDR	a	0.0026
klotho	KL	*	0.0005
Kruppel-like factor 1 (erythroid)	KLF1	a	0.0006
Kruppel-like factor 15	KLF15	*	0.0005
Kruppel-like factor 5	KLF5	a	0.0352
Kruppel-like factor 9	BTEB1	*	0.0005
kynureninase (L-kynurenine hydrolase)	KYNU	a	0.0166
L-3-hydroxyacyl-Coenzyme A dehydrogenase, short chain	HADHSC	*	0.0176
lactate dehydrogenase 1, A chain	LDHA	a	0.0096
laminin B1 subunit 1	LAMB1	a	0.0321
laminin receptor 1 (67kD, ribosomal protein SA)	LAMR1	*	0.0139
laminin, alpha 2	LAMA2	b	
latexin	LXN	a	0.0201
lectin, galactose binding, soluble 3	LGALS3	*	0.0005
lectin, galactose binding, soluble 4	LGALS4	a	0.0295
lectin, galactose binding, soluble 9	LGALS9	a	0.0096
leucine zipper-EF-hand containing transmembrane protein 1	LETM1	*	0.0006
leucocyte specific transcript 1	LY117	b	
leukemia-associated gene	STMN1	a	0.0123

leukotriene C4 synthase	LTC4S	a	0.0058
LIM and SH3 protein 1	LASP1	b	
lipoprotein lipase	LPL	*	0.0008
liver-specific bHLH-Zip transcription factor	Lisch7	b	
low density lipoprotein receptor-related protein 2	LRP2	a	0.0155
low density lipoprotein receptor-related protein 6	LRP6	a	0.0201
LPS-induced TNF-alpha factor	LITAF	*	0.0005
lymphocyte antigen 6 complex, locus A		a	0.0005
lymphocyte antigen 6 complex, locus B	LY6E	*	0.0005
lymphocyte specific 1	LSP1	*	0.0126
lyric (D8Bwg1112e) D segment, Chr 8, Brigham & Women's Genetics 1112 expressed	LYRIC	b	
lysosomal-associated protein transmembrane 4A	LAPTM4A	b	
lysosomal-associated protein transmembrane 4B	LAPTM4B	b	
lysosomal-associated protein transmembrane 5	LAPTM5	b	
lysozyme	LYZ	b	
lysyl oxidase-like	LOXL1	a	0.0008
M.musculus mR for protein expressed at high levels in testis	Tex2	b	
macrophage expressed gene 1	MPEG1	*	0.025
macrophage migration inhibitory factor	MIF	b	
macrophage scavenger receptor 2	Msir2	b	
MAD homolog 5 (Drosophila) / expressed sequence AI451355	MADH5	b	
magi-shi homolog, proliferation-associated (Drosophila)	MAGOH	a	0.0068
major vault protein	MVP	a	0.0013
malate dehydrogenase, soluble	MDH1	*	0.0011
malic enzyme, supertant	ME1	*	0.0005
malonyl-CoA decarboxylase	MLYCD	*	0.0009
mammary tumor integration site 6	EIF3S6	*	0.0102
mannose receptor, C type 1	MRC1	b	
mannose-6-phosphate receptor, cation dependent	M6PR	b	
MARCKS-like protein	MLP	b	
matrix gamma-carboxyglutamate (gla) protein	MGP	*	0.0424
matrix metalloproteinase 14 (membrane-inserted)	MMP14	b	
matrix metalloproteinase 2	MMP2	b	
matrix metalloproteinase 23	MMP23A	b	
matrix metalloproteinase 7	MMP7	b	
max binding protein	MNT	b	
melanoma antigen, family D, 2	MAGED2	*	0.0201
meprin 1 alpha	MEP1A	*	0.0155
metallothionein 1	MT1A	*	0.0047
metallothionein 2	MT2A	a	0.0023
metastasis associated 1-like 1	MTAIL1	b	
methionine aminopeptidase 2	METAP2	a	0.0123
methyl CpG binding protein 2	MECP2	b	
methylene tetrahydrofolate dehydrogenase (DP+ dependent), methenyltetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthase	MTHFD1	*	0.0054
methylmalonyl-Coenzyme A mutase	MUT	*	0.0012
microfibrillar associated protein 5	MGP2	b	

microtubule associated testis specific serine/threonine protein kise	MAST205	a	0.0216
microtubule-associated protein tau	MAPT	a	0.0006
microtubule-associated protein, RP/EB family, member 1	MAPRE1	a	0.0119
mini chromosome maintenance deficient (S. cerevisiae)	MCM3	a	0.0005
mini chromosome maintenance deficient 2 (S. cerevisiae)	MCM2	a	0.0015
mini chromosome maintenance deficient 4 homolog (S. cerevisiae)	MCM4	a	0.0005
mini chromosome maintenance deficient 7 (S. cerevisiae)	MCM7	a	0.039
mitochondrial ribosomal protein L39	MRPL39	a	0.0125
mitochondrial ribosomal protein L50; (D4Wsu125e) D segment, Chr 4, Wayne State University 125, expressed	MRPL50	a	0.0343
Mitogen activated protein kinase 1 ; RIKEN cD 9030612K14 gene	MAPK1	a	0.0439
mitogen activated protein kise 13	MAPK13	a	0.0054
mitogen activated protein kise kise 1	MAP3K1	a	0.0012
mitogen-activated protein kise 7	MAPK7	a	0.025
mitsugumin 29	Mg29	a	0.0389
MORF-related gene X	MORF4L2	a	0.0012
Muf1 protein (D630045E04Rik) Mus musculus, clone IMAGE:3491421, mR, partial cds	MUF1	b	
Mus musculus adult male kidney cD, RIKEN full-length enriched library, clone:0610012C11:homogentisate 1, 2-dioxygese, full insert sequence		a	0.0005
Mus musculus adult male liver cD, RIKEN full-length enriched library, clone:1300015E02:deoxyribonuclease II alpha, full insert sequence	CSAD	a	0.0005
Mus musculus chemokine receptor CCX CKR mR, complete cds, altertively spliced	CCRL1	*	0.0005
Mus musculus evectin-2 (Evt2) mR, complete cds	PLEKHB2	a	0.0005
Mus musculus LDLR dan mR, complete cds		a	0.01
Mus musculus mR for 67 kDa polymerase-associated factor PAF67 (paf67 gene)	EIF3S6IP	a	0.007
Mus musculus mR for alpha-albumin protein	AFM	a	0.0005
Mus musculus, basic transcription factor 3, clone MGC:6799 IMAGE:2648048, mR, complete cds	LOC218490	a	0.0005
Mus musculus, clone IMAGE:3155544, mR, partial cds	LOC224650	a	0.0467
Mus musculus, clone IMAGE:3494258, mR, partial cds		*	0.0009
Mus musculus, clone IMAGE:3586777, mR, partial cds	DLAT	*	0.0019
Mus musculus, clone IMAGE:3589087, mR, partial cds		a	0.0047
Mus musculus, clone IMAGE:3967158, mR, partial cds	C13orf11	a	0.0424
Mus musculus, clone IMAGE:3994696, mR, partial cds	YUP8H12R.13	b	
Mus musculus, clone IMAGE:4456744, mR, partial cds	G630055P03Ri	a	0.0151
Mus musculus, clone IMAGE:4486265, mR, partial cds		a	0.0021
Mus musculus, clone IMAGE:4952483, mR, partial cds	TOR2A	b	
Mus musculus, clone IMAGE:4974221, mR, partial cds	APEH	a	0.0085



Mus musculus, clone MGC:12039 IMAGE:3603661, mR, complete cds	ltp5	a	0.0119
Mus musculus, clone MGC:12159 IMAGE:3711169, mR, complete cds	D530037I19Rik	b	
Mus musculus, clone MGC:18871 IMAGE:4234793, mR, complete cds	GLYAT	(b+b)=b	
Mus musculus, clone MGC:18985 IMAGE:4011674, mR, complete cds	FLJ20303	a	0.0068
Mus musculus, clone MGC:19042 IMAGE:4188988, mR, complete cds	OGDH	a	0.0008
Mus musculus, clone MGC:19361 IMAGE:4242170, mR, complete cds		a	0.0424
Mus musculus, clone MGC:29021 IMAGE:3495957, mR, complete cds	TAO1	a	0.0042
Mus musculus, clone MGC:36388 IMAGE:5098924, mR, complete cds	MCSC	*	0.0233
Mus musculus, clone MGC:36554 IMAGE:4954874, mR, complete cds	D14Ert226e	b	
Mus musculus, clone MGC:36997 IMAGE:4948448, mR, complete cds	MGC36997	a	0.0472
Mus musculus, clone MGC:37818 IMAGE:5098655, mR, complete cds	MGC37818	*	0.004
Mus musculus, clone MGC:38363 IMAGE:5344986, mR, complete cds	TM4SF3	b	
Mus musculus, clone MGC:38798 IMAGE:5359803, mR, complete cds	MGC38798	a	0.0013
Mus musculus, clone MGC:6377 IMAGE:3499365, mR, complete cds	ME2	a	0.024
Mus musculus, clone MGC:6545 IMAGE:2655444, mR, complete cds	MAT2A	a	0.0008
Mus musculus, clone MGC:7898 IMAGE:3582717, mR, complete cds		*	0.0012
Mus musculus, hypothetical protein MGC11287 similar to ribosomal protein S6 k1se, clone MGC:28043 IMAGE:3672127, mR, complete cds	RPS6KL1	a	0.0343
Mus musculus, Similar to 60S ribosomal protein L30 isolog, clone MGC:6735 IMAGE:3590401, mR, complete cds		a	0.0041
Mus musculus, Similar to angiopoietin-like factor, clone MGC:32448 IMAGE:5043159, mR, complete cds		b	
Mus musculus, Similar to CGI-147 protein, clone MGC:25743 IMAGE:3990061, mR, complete cds		*	0.025
Mus musculus, Similar to chromosome 20 open reading frame 36, clone IMAGE:5356821, mR, partial cds	FLJ10883	*	0.0159
Mus musculus, Similar to cortactin isoform B, clone MGC:18474 IMAGE:3981559, mR, complete cds	EMS1	a	0.0018
Mus musculus, Similar to dendritic cell protein, clone MGC:11741 IMAGE:3969335, mR, complete cds	GA17	*	0.019
Mus musculus, Similar to DKFZP586B0621 protein, clone MGC:38635 IMAGE:5355789, mR, complete cds	C1QTNF5	b	
Mus musculus, similar to heterogeneous nuclear ribonucleoprotein A3 (H. sapiens), clone MGC:37309 IMAGE:4975085, mR, complete cds	MGC37309	*	0.0005

Mus musculus, Similar to hypothetical protein DKFZp566A1524, clone MGC:18989 IMAGE:4012217, mR, complete cds	DKFZp566A1524	a	0.013
Mus musculus, Similar to hypothetical protein FLJ10520, clone MGC:27888 IMAGE:3497792, mR, complete cds	FLJ10520	a	0.0005
Mus musculus, Similar to hypothetical protein FLJ12618, clone MGC:28775 IMAGE:4487011, mR, complete cds	FLJ12618	a	0.0013
Mus musculus, Similar to hypothetical protein FLJ13213, clone MGC:28555 IMAGE:4206928, mR, complete cds	FLJ13213	a	0.0063
Mus musculus, Similar to hypothetical protein FLJ20234, clone MGC:37525 IMAGE:4986113, mR, complete cds	FLJ20234	b	
Mus musculus, Similar to hypothetical protein FLJ20245, clone MGC:7940 IMAGE:3584061, mR, complete cds	FLJ20245	b	
Mus musculus, Similar to hypothetical protein FLJ20335, clone MGC:28912 IMAGE:4922274, mR, complete cds	D14Erd813e	a	0.0079
Mus musculus, Similar to hypothetical protein FLJ21634, clone MGC:19374 IMAGE:2631696, mR, complete cds	FLJ21634	*	0.0012
Mus musculus, Similar to hypothetical protein MGC3133, clone MGC:11596 IMAGE:3965951, mR, complete cds	SF3b10	a	0.006
Mus musculus, Similar to hypothetical protein MGC4368, clone MGC:28978 IMAGE:4503381, mR, complete cds	MGC4368	b	
Mus musculus, Similar to KIAA0763 gene product, clone IMAGE:4503056, mR, partial cds	KIAA0763	a	0.0013
Mus musculus, Similar to KIAA1075 protein, clone IMAGE:5099327, mR, partial cds	TENC1	*	0.0016
Mus musculus, Similar to MIPP65 protein, clone MGC:18783 IMAGE:4188234, mR, complete cds	I500032D16Rik	a	0.0021
Mus musculus, Similar to nucleolar cysteine-rich protein, clone MGC:6718 IMAGE:3586161, mR, complete cds --pending	HSA6591	b	
Mus musculus, Similar to Protein P3, clone MGC:38638 IMAGE:5355849, mR, complete cds	DXS253E	b	
Mus musculus, similar to quinone reductase-like protein, clone IMAGE:4972406, mR, partial cds	VAT1	a	0.0005
Mus musculus, similar to R29893_1, clone MGC:37808 IMAGE:5098192, mR, complete cds		a	0.0008
Mus musculus, Similar to RAS p21 protein activator, clone MGC:7759 IMAGE:3498774, mR, complete cds	LOC218397	a	0.0009
Mus musculus, Similar to retinol dehydrogenase type 6, clone MGC:25965 IMAGE:4239862, mR, complete cds	RODH-4	a	0.0005
Mus musculus, Similar to ribosomal protein S20, clone MGC:6876 IMAGE:2651405, mR, complete cds		b	
Mus musculus, Similar to siruin silent mating type information regulation 2 homolog 7 (S. cerevisiae), clone MGC:37560 IMAGE:4987746, mR, complete cds	SIRT7	a	0.0096
Mus musculus, Similar to transgelin 2, clone MGC:6300 IMAGE:2654381, mR, complete cds	TAGLN2	*	0.0005
Mus musculus, Similar to ubiquitin-conjugating enzyme E2 variant 1, clone MGC:7660 IMAGE:3496088, mR, complete cds	UBE2V1	*	0.0013
Mus musculus, Similar to unc93 (C.elegans) homolog B, clone MGC:25627 IMAGE:4209296, mR, complete cds	UNC93B1	b	
Mus musculus, Similar to xylulokinase homolog (H. influenzae), clone IMAGE:5043428, mR, partial cds		*	0.0012

mutS homolog 2 (E. coli)	MSH2	a	0.0324
mutS homolog 6 (E. coli)	MSH6	a	0.0012
MYB binding protein (P160) 1a	MYBBP1A	a	0.0005
MYC-associated zinc finger protein (purine-binding transcription factor)	MAZ	a	0.0031
myelocytomatosis oncogene	MYC	*	0.0012
myeloid differentiation primary response gene 88	MYD88	b	
myeloid-associated differentiation marker	MYADM	a	0.0005
myocyte enhancer factor 2A	MEF2A	b	
myosin lc	MYO1C	a	0.0047
myosin light chain, alkali, cardiac atria	MYLA	a	0.0005
myosin light chain, alkali, nonmuscle	MYL6	b	
myristoylated alanine rich protein kase C substrate	MACS	b	
N-acetylglucosamine kase	NAGK	a	0.0083
N-acetylneuramite pyruvate lyase	C1orf13	a	0.0068
NCK-associated protein 1	NCKAP1	b	
nestin --pendin	NES	a	0.0308
neural precursor cell expressed, developmentally down-regulated gene 4a	NEDD4	b	
neural proliferation, differentiation and control gene 1	NPDC1	*	0.0042
neuro1 guanine nucleotide exchange factor	NGEF	a	0.0119
neuropilin	NRP1	b	
neutrophil cytosolic factor 2	NCF2	a	0.0424
Ngfi-A binding protein 2	NAB2	b	
nicotinamide nucleotide transhydrogase	NNT	*	0.0047
nidogen 1	NID	b	
NIMA (never in mitosis gene a)-related expressed kase 6	NEK6	a	0.0012
N-myc downstream regulated 2	NDRG2	*	0.0005
non-catalytic region of tyrosine kase adaptor protein 1	NCK1	b	
nuclear factor of kappa light chain gene enhancer in B-cells 1, p105	NFKB1	b	
nuclear protein 15.6	P17.3	a	0.0416
nuclear receptor coactivator 4	NCOA4	b	
nuclear receptor subfamily 2, group F, member 2	NR2F2	b	
nuclear receptor subfamily 2, group F, member 6	NR2F6	b	
nuclease sensitive element binding protein 1	NSEP1	a	0.0005
nucleophosmin 1	NPM1	*	0.0032
numb gene homolog (Drosophila)	NUMB	a	0.0005
oncostatin receptor	OSMR	*	0.0021
opioid growth factor receptor	OGFR	a	0.0207
ornithine aminotransferase	OAT	b	
ornithine decarboxylase, structural	ODC1	a	0.0032
osteomodulin	OMD	a	0.025
oxysterol binding protein-like 1A	OSBPL1A	*	0.0481
pantophysin	HLF	*	0.0008
papillary rel cell carcinoma (translocation-associated)	PRCC	b	
parvalbumin	PVALB	a	0.0026
PC4 and SFRS1 interacting protein 2 (expressed sequence AU015605)	PSIP2	a	0.0431
PCTAIRE-motif protein kase 3	PCTK3	a	0.0396
peptidylprolyl isomerase (cyclophilin)-like 1	PPIL1	a	0.0424

peptidylprolyl isomerase C	PPIC	a	0.0031
peptidylprolyl isomerase C-associated protein	LGALS3BP	b	
period homolog 1 (Drosophila)	PER1	(b+b)=b	
period homolog 2 (Drosophila)	PER2	b	
peroxiredoxin 5	PRDX5	a	0.009
peroxisomal biogenesis factor 13	PEX13	a	0.0031
peroxisomal delta3, delta2-enoyl-Coenzyme A isomerase	PECI	a	0.004
peroxisomal membrane protein 2, 22 kDa	PXMP2	a	0.0008
peroxisomal sarcosine oxidase	PIPOX	a	0.0147
peroxisome proliferator activated receptor alpha	PPARA	a	0.0018
PH domain containing protein in reti 1	PHRET1	a	0.0005
phenylalanine hydroxylase	PAH	*	0.0033
phenylalkylamine Ca2+ antagonist (emopamil) binding protein	EBP	a	0.0023
phorbol-12-myristate-13-acetate-induced protein 1	PMAIP1	*	0.0026
phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 1 (p85 alpha)	PIK3R1	a	0.0381
phosphatidylinositol transfer protein	PTIPN	a	0.0008
phosphodiesterase 1A, calmodulin-dependent	PDE1A	a	0.0361
phosphofructokinase, liver, B-type	PFKL	a	0.0482
phosphoglycerate kinase 1	PGK1	a	0.0403
phosphoglycerate mutase 2	PGAM2	*	0.0005
phospholipase A2, activating protein	PLAA	a	0.03
phospholipase A2, group IB, pancreas	PLA2G1B	a	0.0027
phospholipase A2, group IIA (platelets, synovial fluid)	PLA2G2A	a	0.0017
phospholipid scramblase 1	PLSCR1	a	0.0005
phosphoprotein enriched in astrocytes 15	PEA15	a	0.0008
phytanoyl-CoA hydroxylase	PHYH	a	0.0012
plasminogen activator, tissue	PLAT	b	
platelet derived growth factor receptor, beta polypeptide	PDGFRB	a	0.0026
platelet derived growth factor, alpha	PDGFA	b	
platelet derived growth factor, B polypeptide	PDGFB	b	
platelet factor 4	PF4	*	0.0018
platelet-activating factor acetylhydrolase, isoform 1b, alpha1 subunit	PAFAH1B3	b	
poliovirus receptor-related 3	PVRL3	(a+a)=a	0.03; 0.0337
poly (A) polymerase alpha	PAPOLA	*	0.001
poly(rC) binding protein 1	PCBP1	a	0.0472
polycystic kidney disease 1 homolog	PKD1	a	0.0316
polymerase, gamma	POLG	b	
polypyrimidine tract binding protein 1	PTBP1	a	0.0381
potassium channel, subfamily K, member 2	KCNK2	a	0.0096
PPAR gamma coactivator-1beta protein	PERC	a	0.0029
prion protein	PRNP	b	
procollagen lysine, 2-oxoglutarate 5-dioxygenase 2	PLOD2	a	0.001
procollagen, type I, alpha 1	COL1A1	b	

procollagen, type I, alpha 2	COL1A2	b	
procollagen, type IV, alpha 1	COL4A1	*	0.0005
procollagen, type IV, alpha 2	COL4A2	b	
procollagen, type V, alpha 1	COL5A1	a	0.0017
procollagen, type V, alpha 2	COL5A2	*	0.0005
prohibitin	PHB	a	0.0165
proline dehydrogenase	PRODH	*	0.0018
protease (prosome, macropain) 26S subunit, ATPase 1	PSMC1	a	0.0047
proteasome (prosome, macropain) 28 subunit, 3	PSME3	a	0.0014
proteasome (prosome, macropain) 26S subunit, non-ATPase, i0	PSMD10	a	0.0422
proteasome (prosome, macropain) 26S subunit, non-ATPase, i3	PSMD13	a	0.0086
proteasome (prosome, macropain) 28 subunit, alpha	PSME1	*	0.0012
proteasome (prosome, macropain) subunit, alpha type 2	PSMA2	a	0.0009
proteasome (prosome, macropain) subunit, alpha type 6	PSMA6	a	0.0248
proteasome (prosome, macropain) subunit, alpha type 7	PSMA7	b	
proteasome (prosome, macropain) subunit, beta type 1	PSMB1	b	
proteasome (prosome, macropain) subunit, beta type 10	PSMB10	b	
protein C	PROC	a	0.0014
protein kise C, delta	PRKCD	b	
protein phosphatase 1, catalytic subunit, alpha isoform	PPP1CA	a	0.0005
protein phosphatase 1, regulatory (inhibitor) subunit 1A	PPP1R1A	a	0.0005
protein phosphatase 2a, catalytic subunit, beta isoform	PPP2CB	a	0.0014
protein phosphatase 3, catalytic subunit, gamma isoform	PPP3CC	a	0.0086
protein S (alpha)	PROS1	b	
protein tyrosine phosphatase 4a1	PTP4A1	a	0.004
protein tyrosine phosphatase, non-receptor type 9	PTPN9	*	0.0454
protein tyrosine phosphatase, receptor type, B	PTPRB	a	0.0497
protein tyrosine phosphatase, receptor type, C	PTPRC	*	0.0481
protein tyrosine phosphatase, receptor type, C polypeptide-associated protein	PTPRCAP	b	
protein tyrosine phosphatase, receptor type, O	PTPRO	b	
proteoglycan, secretory granule	PRG1	a	0.0005
proteasome (prosome, macropain) subunit, beta type 8 (large multifunctional protease 7)	PSMB8	b	
prothymosin alpha	PTMA	*	0.005
purinergic receptor (family A group 5) ; RIKEN cDNA 2610302I02 gene	P2RY5	b	
pyridoxal (pyridoxine, vitamin B6) kise	PDXK	a	0.0096
PYRIN-containing APAF1-like protein 5 / expressed sequence A1504961	PYPAF5	b	
pyruvate decarboxylase	PC	b	
pyruvate dehydrogenase 2	PDK2	a	0.0005
pyruvate kise 3	PKM2	a	0.0005
pyruvate kise liver and red blood cell	PKLR	*	0.031
R binding motif protein 3	RBM3	*	0.0005
R polymerase I associated factor, 53 kD	PAF53	a	0.0012
R polymerase II 1	POLR2A	a	0.0497
RAB11a, member RAS oncogene family	RAB11A	a	0.0086
RAB3D, member RAS oncogene family	RAB3D	b	

Ral-interacting protein 1	RALBP1	a	0.0063
RAN, member RAS oncogene family	RAN	a	0.0005
Rap1, GTPase-activating protein 1	RAP1GA1	a	0.0023
RAR-related orphan receptor alpha	RORA	b	
ras homolog 9 (RhoC)	ARHC	*	0.0005
ras homolog B (RhoB)	ARHB	*	0.0202
ras homolog D (RhoD)	ARHD	b	
ras homolog gene family, member E	ARHE	a	0.0023
Ras-GTPase-activating protein (GAP<120>) SH3-domain binding protein 2	G3BP2	a	0.03
RAS-related C3 botulinum substrate 2	RAC2	b	
reduced expression 3	BEX1	b	
regulator for ribosome resistance homolog (S. cerevisiae)	RRS1	a	0.0013
regulator of G-protein sigling 14	RGS14	*	0.0018
regulator of G-protein sigling 19 interacting protein 1	RGS19IP1	a	0.0068
renin 2 tandem duplication of Ren1	Ren2	b	
reticulocalbin	RCN1	a	0.0009
reticulin 3	RTN3	a	0.0096
retinoblastoma binding protein 4	RBBP4	b	
retinoblastoma binding protein 7	RBBP7	a	0.0005
retinoblastoma-like 1 (p107)	RBL1	a	0.0057
retinoic acid early transcript gamma		b	
retinoic acid induced 1	RAI1	a	0.0111
retinol binding protein 1, cellular	RBP1	b	
Rhesus blood group-associated C glycoprotein	RHCG	a	0.0064
Rho guanine nucleotide exchange factor (GEF) 3	ARHGEF3	a	0.0023
ribonucleotide reductase M1	RRM1	a	0.0037
ribosomal protein L10A	RPL10A	*	0.0005
ribosomal protein L12	RPL12	b	
ribosomal protein L13a	RPL13A	a	0.0005
ribosomal protein L18	RPL18	b	
ribosomal protein L19	RPL19	*	0.0005
ribosomal protein L21	RPL21	a	0.0005
ribosomal protein L27a	RPL27A	*	0.0008
ribosomal protein L28	RPL28	a	0.0012
ribosomal protein L29	RPL29	*	0.0005
ribosomal protein L3	RPL3	*	0.0006
ribosomal protein L35	RPL35	*	0.0009
ribosomal protein L36	RPL36	a	0.0005
ribosomal protein L41	RPL41	a	0.0005
ribosomal protein L44	RPL36A	*	0.0011
ribosomal protein L5	RPL5	*	0.0005
ribosomal protein L6	RPL6	*	0.0005
ribosomal protein L7	RPL7	b	
ribosomal protein L8	RPL8	a	0.0182
ribosomal protein S14	RPS14	b	
ribosomal protein S15	SYN1	*	0.0005

ribosomal protein S15	RPS15	a	0.0009
ribosomal protein S16	RPS16	*	0.0005
ribosomal protein S19	RPS19	a	0.0005
ribosomal protein S2	RPS2	a	0.0008
ribosomal protein S23	RPS23	*	0.0006
ribosomal protein S26	RPS26	a	0.0017
ribosomal protein S29	RPS29	b	
ribosomal protein S3	RPS3	a	0.0009
ribosomal protein S3a	RPS3A	*	0.0005
ribosomal protein S4, X-linked	RPS4X	*	0.0005
ribosomal protein S5	RPS5	b	
ribosomal protein S6	RPS6	(*+*)=* 0.0005;	0.0005
ribosomal protein S6 kisc, 90kD, polypeptide 4	RPS6KA4	a	0.0211
ribosomal protein S7	RPS7	*	0.0005
ribosomal protein, large P2	RPLP2	b	
ribosomal protein, large, P1	RPLP1	*	0.0005
RIKEN cD 0610006F02 gene	DKFZP566H073	(b+b)=b	
RIKEN cD 0610006N12 gene	NDUFB4	a	0.0163
RIKEN cD 0610007L01 gene	FLJ10099	a	0.008
RIKEN cD 0610011C19 gene	FLJ22386	a	0.0077
RIKEN cD 0610016J10 gene	CGI-27	a	0.0014
RIKEN cD 0610025G13 gene	RPL38	*	0.0023
RIKEN cD 0610025I19 gene	0610025I19Rik	*	0.0005
RIKEN cD 0610041E09 gene	AD-020	a	0.0042
RIKEN cD 1010001M04 gene	1010001M04Rik	a	0.0005
RIKEN cD 1100001F19 gene	UBE2D3	a	0.0048
RIKEN cD 1100001J13 gene -pending	KIAA1049	a	0.0296
RIKEN cD 1110001I24 gene	BZW2	*	0.0025
RIKEN cD 1110002C08 gene	MGC9564	a	0.0497
RIKEN cD 1110005N04 gene	TAF5L	b	
RIKEN cD 1110007F23 gene	1110007F23Rik	b	
RIKEN cD 1110008B24 gene	C14orf111	b	
RIKEN cD 1110014C03 gene	TMP21	a	0.0008
RIKEN cD 1110020L19 gene	TREX2	a	0.0422
RIKEN cD 1110032A13 gene	FLJ21172	b	
RIKEN cD 1110038J12 gene		*	0.0068
RIKEN cD 1110038L14 gene	CKS2	a	0.0086
RIKEN cD 1110054A24 gene	1110054A24Rik	a	0.0335
RIKEN cD 1190006C12 gene	SEC61B	b	
RIKEN cD 1200003E16 gene	1200003E16Rik	a	0.004
RIKEN cD 1200009B18 gene	LOC51290	b	
RIKEN cD 1200011D11 gene	BK65A6.2	a	0.0005
RIKEN cD 1200013A08 gene	MGC3047	b	
RIKEN cD 1200014D15 gene	DMGDH	*	0.0006

RIKEN cD 1200014I03 gene	F13A1	a	0.0015
RIKEN cD 1200015A22 gene	MGC3222	a	0.0119
RIKEN cD 1200016G03 gene	1200016G03Rik	a	0.0012
RIKEN cD 1300002P22 gene	ECH1	a	0.0013
RIKEN cD 1300004O04 gene	CACH-1	*	0.0068
RIKEN cD 1300013F15 gene	FLJ22390	b	
RIKEN cD 1300013G12 gene	1300013G12Rik	a	0.0072
RIKEN cD 1300017C12 gene	FLJ10948	a	0.0011
RIKEN cD 1300018I05 gene	KIAA0082	a	0.0472
RIKEN cD 1300019I21 gene	MTAP	a	0.0012
RIKEN cD 1500010B24 gene	EIF1A	(b+b)=b	
RIKEN cD 1500026A19 gene	ALG5	a	0.0189
RIKEN cD 1500041J02 gene	FLJ13448	*	0.0497
RIKEN cD 1700008H23 gene	1700008H23Rik	b	
RIKEN cD 1700012B18 gene	OKL38	a	0.0381
RIKEN cD 1700015P13 gene	1700015P13Rik	b	
RIKEN cD 1700016A15 gene	FLJ11806	b	
RIKEN cD 1700028A24 gene	LOC55862	a	0.0096
RIKEN cD 1700037H04 gene	FLJ20550	a	0.0381
RIKEN cD 1810009M01 gene	LR8	a	0.0005
RIKEN cD 1810013B01 gene	1810013B01Rik	a	0.0015
RIKEN cD 1810023B24 gene	FLJ14503	a	0.0424
RIKEN cD 1810027P18 gene	DCXR	a	0.0013
RIKEN cD 1810036E22 gene		a	0.004
RIKEN cD 1810038D15 gene	DKFZP566E144	a	0.0096
RIKEN cD 1810043O07 gene	KIAA0601	b	
RIKEN cD 1810054O13 gene	1810054O13Rik	a	0.0005
RIKEN cD 1810058K22 gene	CDC42EP1	a	0.0009
RIKEN cD 2010012D11 gene	2010012D11Rik	*	0.0065
RIKEN cD 2010315L10 gene	MDS032	a	0.006
RIKEN cD 2310001A20 gene	C20orf3	a	0.0012
RIKEN cD 2310004I03 gene	2310004I03Rik	a	0.0482
RIKEN cD 2310004L02 gene	FLJ10241	*	0.0006
RIKEN cD 2310009E04 gene	FLJ10986	*	0.0005
RIKEN cD 2310010G13 gene	2310010G13Rik	a	0.025
RIKEN cD 2310022K15 gene	KLHDC2	b	
RIKEN cD 2310032J20 gene	BDH	a	0.0032
RIKEN cD 2310046G15 gene	SPUVE	b	
RIKEN cD 2310051E17 gene	2310051E17Rik	a	0.0005
RIKEN cD 2310067B10 gene	KIAA0195	a	0.0452



RIKEN cD 2310075M15 gene	2310075M15Rik	(a+*)=*	0.0099
RIKEN cD 2310079C17 gene	DKFZP547E2110	a	0.0154
RIKEN cD 2410002J21 gene	ENIGMA	a	0.0309
RIKEN cD 2410021P16 gene	MGC5601	a	0.0012
RIKEN cD 2410026K10 gene	CD99	b	
RIKEN cD 2410029D23 gene	ATP6V1E1	a	0.0162
RIKEN cD 2410129E14 gene		b	
RIKEN cD 2410174K12 gene	SUGT1	b	
RIKEN cD 2510015F01 gene	FLJ12442	a	0.0005
RIKEN cD 2600001N01 gene	ZWINT	a	0.0013
RIKEN cD 2600015J22 gene		b	
RIKEN cD 2600017H24 gene		a	0.0331
RIKEN cD 2610007A16 gene	SEC13L	a	0.0005
RIKEN cD 2610029K21 gene	FLJ20249	a	0.0126
RIKEN cD 2610039E05 gene	2610039E05Rik	a	0.0046
RIKEN cD 2610200M23 gene	SSBP3	b	
RIKEN cD 2610206D03 gene	2610206D03Rik	a	0.0018
RIKEN cD 2610301D06 gene	2610301D06Rik	a	0.0005
RIKEN cD 2610305D13 gene	FLJ11191	a	0.0009
RIKEN cD 2610306D21 gene	ANAPC4	b	
RIKEN cD 2610511O17 gene	FLJ20272	a	0.0157
RIKEN cD 2610524G07 gene		a	0.0013
RIKEN cD 2610524G09 gene	IER5	a	0.0491
RIKEN cD 2700027J02 gene	SPF45	a	0.0243
RIKEN cD 2700038K18 gene		b	
RIKEN cD 2700038M07 gene -pending	WSB1	b	
RIKEN cD 2700055K07 gene	CGI-38	b	
RIKEN cD 2700099C19 gene	LOC51248	a	0.0057
RIKEN cD 2810004N23 gene	2810004N23Rik	a	0.0073
RIKEN cD 2810047L02 gene	RAMP	a	0.004
RIKEN cD 2810409H07 gene	PTD004	a	0.0018
RIKEN cD 2810411G23 gene	TPD52L2	a	0.0026
RIKEN cD 2810418N01 gene	KIAA0186	b	
RIKEN cD 2810430J06 gene	FRCP1	b	
RIKEN cD 2810468K17 gene	MGC13272	b	
RIKEN cD 2810473M14 gene	2810473M14Rik	a	0.0139
RIKEN cD 2900074L19 gene		b	
RIKEN cD 3010001A07 gene	BFAR	a	0.0244
RIKEN cD 3010027G13 gene	DKFZp434C119.1	a	0.0008
RIKEN cD 3021401A05 gene	3021401A05Rik	*	0.006
RIKEN cD 3110001N18 gene	RPI.22	b	
RIKEN cD 3230402E02 gene	FLJ10983	a	0.0201
RIKEN cD 3321401G04 gene	KIAA0738	b	

RIKEN cD 4430402G14 gene	H3f3b	*	0.0012
RIKEN cD 4632401C08 gene	4632401C08Rik	a	0.0005
RIKEN cD 4733401N12 gene	CPSF6	b	
RIKEN cD 4921528E07 gene	4921528E07Rik	b	
RIKEN cD 4921537D05 gene	NY-REN-58	a	0.033
RIKEN cD 4930506M07 gene	FLJ11122	a	0.03
RIKEN cD 4930533K18 gene		*	0.0005
RIKEN cD 4930542G03 gene	4930542G03Rik	a	0.0005
RIKEN cD 4930552N12 gene	MCCC2	*	0.0009
RIKEN cD 4930579A11 gene	VMP1	a	0.0023
RIKEN cD 4932442K08 gene	4932442K08Rik	b	
RIKEN cD 4933405K01 gene	MGC14799	a	0.0037
RIKEN cD 5031412I06 gene	Dutp	a	0.0068
RIKEN cD 5031422I09 gene	PKP4	*	0.0023
RIKEN cD 5133400A03 gene	5133400A03Rik	*	0.0005
RIKEN cD 5133401H06 gene	5133401H06Rik	a	0.0008
RIKEN cD 5430416A05 gene	AD034	a	0.024
RIKEN cD 5630401J11 gene	5630401J11Rik	b	
RIKEN cD 5730403B10 gene	C16orf5	a	0.0092
RIKEN cD 5730406I15 gene	KIAA0102	b	
RIKEN cD 5730534O06 gene	KIAA0164	a	0.0006
RIKEN cD 5830445O15 gene	5830445O15Rik	a	0.0119
RIKEN cD 6230410I01 gene	FLJ10849	b	
RIKEN cD 6330565B14 gene	ADH8	*	0.0009
RIKEN cD 6330583M11 gene	DKFZP434P106	*	0.0005
RIKEN cD 6430559E15 gene	HT036	a	0.0008
RIKEN cD 6530411B15 gene	DKFZp564K1964.1	*	0.0086
RIKEN cD 6720463E02 gene		a	0.0047
RIKEN cD 9130011J04 gene	9130011J04Rik	b	
RIKEN cD 9130022E05 gene	9130022E05Rik	a	0.0353
RIKEN cD 9530058B02 gene	MGC15416	*	0.0005
RIKEN cD 9530089B04 gene	9530089B04Rik	*	0.0023
RIKEN cD A230106A15 gene	A230106A15Rik	a	0.0424
RIKEN cD A330103N21 gene	A330103N21Rik	(a+a)=a	0.0012; 0.0072
RIKEN cD A930008K15 gene	KIAA0605	a	0.0054
RIKEN cD D630002J15 gene	D630002J15Rik	a	0.0068

RIKEN cD E130113K08 gene	T50835	b	
ring finger protein (C3HC4 type) 19	RNF19	b	
runt related transcription factor 1	RUNX1	b	
S100 calcium binding protein A10 (calpactin)	S100A10	*	0.0005
S100 calcium binding protein A13	S100A13	b	
S100 calcium binding protein A4	S100A4	*	0.0026
S100 calcium binding protein A6 (calcyclin)	S100A6	*	0.0005
S-adenosylhomocysteine hydrolase	AHCY	b	
SAR1a gene homolog (S. cerevisiae)	SAR1	a	0.0018
schlafen 4	FLJ10260	a	0.0023
SEC13 related gene (S. cerevisiae) RIKEN cD 1110003H02 gene	SEC13L1	a	0.0096
SEC61, gamma subunit (S. cerevisiae)	SEC61G	a	0.0081
secreted acidic cysteine rich glycoprotein	SPARC	*	0.0005
secreted and transmembrane 1	SECTM1	b	
secreted phosphoprotein 1	SPP1	a	0.0005
selectin, platelet (p-selectin) ligand	SELPLG	b	
selenium binding protein 2	SELENBP1	b	
selenophosphate synthetase 2	SPS2	b	
selenoprotein P, plasma, 1	SEPP1	a	0.0086
septin 8	KIAA0202	a	0.025
serine (or cysteine) protease inhibitor, clade B (ovalbumin), member 2	SERPINB2	a	0.0013
serine (or cysteine) protease inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	SERPINE2	b	
serine (or cysteine) protease inhibitor, clade G (C1 inhibitor), member 1	SERPING1	b	
serine (or cysteine) protease inhibitor, clade H (heat shock protein 47), member 1	SERPINH1	*	0.0005
serine hydroxymethyl transferase 1 (soluble)	SHMT1	b	
serine hydroxymethyl transferase 2 (mitochondrial); RIKEN cD 2700043D08 gene	SHMT2	*	0.0005
serine palmitoyltransferase, long chain base subunit 1	SPITLC1	a	0.0422
serine protease inhibitor 6	SERPINB9	b	
serine protease inhibitor, Kunitz type 1	SPINT1	a	0.0011
serine protease inhibitor, Kunitz type 2	SPINT2	a	0.0071
serine/arginine repetitive matrix 1	RAD23B	a	0.0068
serine/threonine kinase receptor associated protein	UNRIP	a	0.0119
serine/threonine protein kinase CISK	SGKL	a	0.0424
serum amyloid A 3	SAA3P	a	0.0008
serum/glucocorticoid regulated kinase	SGK	b	
serum/glucocorticoid regulated kinase 2	SGK2	*	0.0006
SET translocation	SET	a	0.005
sex-lethal interactor homolog (Drosophila)	RPC5	*	0.0058
SFFV proviral integration 1	SP11	b	
SH3 domain binding glutamic acid-rich protein-like 3	SH3BGR13	*	0.0005
SH3 domain protein 3	OSTF1	a	0.0037
sideroflexin 1	SFXN1	a	0.0201
sigl sequence receptor, delta	SSR4	*	0.0023
sigl transducer and activator of transcription 3	STAT3	b	
sigling intermediate in Toll pathway-evolutionarily conserved	Sitpec	b	
single Ig IL-1 receptor related protein	SIGIRR	b	

slit homolog 2 (Drosophila)	SLIT2	a	0.0057
slit homolog 3 (Drosophila)	SLIT3	b	
small inducible cytokine A2	SCYA2	*	0.0008
small inducible cytokine A5	SCYA5	b	
small inducible cytokine A7	SCYA7	b	
small inducible cytokine A9	CCL9	*	0.0016
small inducible cytokine B subfamily (Cys-X-Cys), member 10	SCYB10	*	0.0005
small inducible cytokine B subfamily, member 5	SCYB6	b	
small inducible cytokine subfamily D, 1	SCYD1	*	0.0091
small nuclear ribonucleoprotein D2	SNRPD2	*	0.0116
small nuclear ribonucleoprotein E	SNRPE	b	
small nuclear ribonucleoprotein polypeptide G	SNRPG	*	0.0042
small proline-rich protein 1A	SPRR1A	b	
SMC (structural maintenance of chromosomes 1)-like 1 (S. cerevisiae)	SMC1L1	a	0.0018
smoothelin	SMTN	a	0.0005
smoothened homolog (Drosophila)	SMOII	b	
soc-2 (suppressor of clear) homolog (C. elegans)	SHOC2	b	
solute carrier family 1, member 1	SLC1A1	b	
solute carrier family 12, member 1	SLC12A1	a	0.0023
solute carrier family 13 (sodium/sulphate symporters), member 1	SLC13A1	*	0.0021
solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3	SLC13A3	*	0.0047
solute carrier family 15 (H <sup>+</sup> /peptide transporter), member 2	SLC15A2	a	0.0037
solute carrier family 16 (monocarboxylic acid transporters), member 2	SLC16A2	a	0.0058
solute carrier family 16 (monocarboxylic acid transporters), member 7	SLC16A7	b	
solute carrier family 2 (facilitated glucose transporter), member 5	SLC2A5	b	
solute carrier family 22 (organic anion transporter), member 6	SLC22A6	b	
solute carrier family 22 (organic anion transporter), member 8 / (Roct) reduced in osteosclerosis transporter	SLC22A8	*	0.0005
solute carrier family 22 (organic cation transporter), member 1	SLC22A1	*	0.0009
solute carrier family 22 (organic cation transporter), member 1-like	SLC22A1L	*	0.0005
solute carrier family 22 (organic cation transporter), member 2	SLC22A2	*	0.0005
solute carrier family 22 (organic cation transporter), member 4	SLC22A4	b	
solute carrier family 22 (organic cation transporter), member 5	SLC22A5	*	0.0015
solute carrier family 22 (organic cation transporter)-like 2	SLC22A2	a	0.0088
solute carrier family 25 (mitochondrial carrier)	SLC25A10	a	0.0005
solute carrier family 25 (mitochondrial carrier)	SLC25A13	b	
solute carrier family 25 (mitochondrial deoxynucleotide carrier), member 19	SLC25A19	a	0.0005
solute carrier family 26, member 4	SLC26A4	*	0.033
solute carrier family 27 (fatty acid transporter), member 2	SLC27A2	*	0.0146
solute carrier family 3, member 1	SLC3A1	b	
solute carrier family 31, member 1	SLC31A1	a	0.0206
solute carrier family 34 (sodium phosphate), member 1	SLC34A1	a	0.005
solute carrier family 34 (sodium phosphate), member 2	SLC34A2	b	
solute carrier family 35, member A5; RIKEN cD 1010001J06	SLC35A5	a	0.0026

gene			
solute carrier family 4 (anion exchanger), member 4	SLC4A4	*	0.0221
solute carrier family 6 (neurotransmitter transporter, glycine), member 9 / glycine transporter 1	SLC6A9	a	0.0225
solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> -system), member 7	SLC7A7	*	0.025
solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> -system), member 9	SLC7A9	*	0.0008
speckle-type POZ protein	SPOP	a	0.0135
spermatogenesis associated factor	SPATA5	a	0.0189
spermidine synthase	SRM	a	0.0026
spermidine/spermine N1-acetyl transferase	SAT	b	
sphingomyelin phosphodiesterase 2, neutral	SMPD2	a	0.0047
splicing factor 3b, subunit 1, 155 kDa	SF3B1	*	0.0162
splicing factor, arginine/serine-rich 2 (SC-35)	SFRS2	a	0.0011
split hand/foot deleted gene 1	DSS1	b	
src homology 2 domain-containing transforming protein D	SHD	a	0.027
src-like adaptor protein	SLA	a	0.0183
stearoyl-Coenzyme A desaturase 1	SCD	*	0.0008
steroid receptor R activator 1	SRA1	a	0.0012
sterol carrier protein 2, liver	SCP2	*	0.0008
striatin, calmodulin binding protein 4 / expressed sequence C80611	STRN4	b	
stromal cell derived factor 1	CXCL12	a	0.0012
succinate dehydrogenase complex, subunit B, iron sulfur (Ip); RIKEN cD710008N11 gene	SDHB	a	0.0011
succinate dehydrogenase complex, subunit A, flavoprotein (Fp)	SDHA	a	0.0006
succinate-Coenzyme A ligase, ADP-forming, beta subunit	SUCLA2	a	0.0015
succinate-Coenzyme A ligase, GDP-forming, beta subunit	SUCLG2	a	0.0197
sulfotransferase-related protein SULT-X1	Sult-x1	b	
superoxide dismutase 2, mitochondrial	SOD2	*	0.0005
surfeit gene 4	SURF4	a	0.0058
SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5	SMARCA5	(a+a)=a	0.0183; 0.0166
SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily e, member 1	SMARCE1	a	0.0013
syndecan 1	SDC1	a	0.0008
syntrophin, basic 2	SNTB2	a	0.0197
TAF10 R polymerase II, TATA box binding protein (TBP)-associated factor, 30 kDa	TAF10	a	0.0006
TAF9 R polymerase II, TATA box binding protein (TBP)-associated factor, 32 kDa	TAF9	a	0.0178
talín 2	TLN2	*	0.0005
TATA box binding protein-like protein	TBPL1	b	
T-box 6	TBX6	*	0.0497
T-cell specific GTPase	Tgtp	b	
T-cell, immune regulator 1	TCIRG1	b	
TEA domain family member 2	TEAD2	a	0.0112
tescín C	TNC	*	0.0005
tescín XB	TNXB	a	0.036
testis derived transcript	TES	a	0.0018
tetranectin (plasminogen binding protein)	TNA	a	0.0204

tetrapeptide repeat domain	TTC3	b	
TG interacting factor	TGIF	*	0.006
thiamin pyrophosphokise	TPK1	a	0.0078
thioesterase, adipose associated	THEA	*	0.0119
thioether S-methyltransferase	Temt	b	
thioredoxin 1	TXN	*	0.0009
thioredoxin 2	TXN2	b	
thioredoxin-like (32kD)	TXNL	a	0.0023
thrombospondin 1	THBS1	b	
thymidine kise 1	TK1	a	0.0245
thymoma viral proto-oncogene 1	AKT1	a	0.0005
thymosin, beta 4, X chromosome	TMSB4X	*	0.0005
thyroid hormone responsive SPOT14 homolog (Rattus)	THRSP	*	0.001
Tial1 cytotoxic granule-associated R binding protein-like 1	ITAL1	a	0.01
tight junction protein 2	TJP2	b	
tissue inhibitor of metalloproteinase	TIMP1	*	0.0005
Tnf receptor-associated factor 2	TRAF2	a	0.0037
toll-like receptor 2	TLR2	b	
topoisomerase (D) III beta	TOP3B	a	0.0186
TRAF-interacting protein	TRIP	a	0.004
transcobalamin 2	TCN2	*	0.0012
transcription elongation factor A (SII), 3	TCEA3	a	0.0068
transcription elongation regulator 1 (CA150)	TCERG1	*	0.0005
transcription factor 21	TCF21	b	
transcription factor 4	TCF4	b	
transcription factor Dp 1	TFDP1	b	
transformation related protein 53	TP53	a	0.0005
transformed mouse 3T3 cell double minute 2	MDM2	b	
transforming growth factor beta 1 induced transcript 4	TSC22	*	0.0012
transforming growth factor, beta induced, 68 kDa	TGFB1	*	0.0005
transgelin	TAGLN	*	0.0173
translin	TSN	a	0.004
transmembrane 7 superfamily member 1	TM7SF1	a	0.0023
transmembrane protein 8 (five membrane-spanning domains)	TMEM8	(*+a)=*	0.0219; 0.0026
Trans-prenyltransferase	Trpt	b	
transthyretin	TTR	a	0.0086
trinucleotide repeat containing 11 (THR-associated protein, 230 kDa subunit)	TNRC11	b	
tropomyosin 2, beta	TPM2	a	0.0005
tropomyosin 3, gamma	TPM3	*	0.0005
tubulin alpha 1	TUBA1	b	
tubulin alpha 2	TUBA2	*	0.0005
tubulin, beta 5	TUBB	a	0.0005
tuftelin 1	TUFT1	a	0.004
tumor necrosis factor receptor superfamily, member 10b	TNFRSF10B	a	0.0198
tumor necrosis factor receptor superfamily, member 1a	TNFRSF1A	*	0.018
tumor necrosis factor receptor superfamily, member 1b	TNFRSF1B	b	

tumor protein p53 binding protein, 2 / expressed sequence AI746547	TP53BP2	b	
tumor rejection antigen gp96	TRA1	a	0.0103
tumor-associated calcium sig1 transducer 2	TACSTD2	*	0.0005
tural killer tumor recognition sequence	NKTR	*	0.0022
TYRO protein tyrosine kase binding protein	TYROBP	*	0.0008
tyrosine 3-monooxygese/tryptophan 5-monooxygese activation protein, epsilon polypeptide	YWHAH	a	0.0006
tyrosine 3-monooxygese/tryptophan 5-monooxygese activation protein, eta polypeptide	YWHAH	*	0.0005
ubiquitin specific protease 2	USP2	*	0.0005
ubiquitin specific protease 7 (expressed sequence AA409944)	USP7	a	0.0005
ubiquitin-conjugating enzyme E2D 2	UBE2D2	b	
ubiquitin-conjugating enzyme E2H	UBE2H	*	0.0068
ubiquitin-conjugating enzyme E2I	UBE2I	a	0.0005
ubiquitin-conjugating enzyme E2L 3	UBE2L3	a	0.0072
ubiquitin-conjugating enzyme E2N	UBE2N	*	0.0009
ubiquitin-like 1	UBL1	a	0.0381
ubiquitin-like 1 (sentrin) activating enzyme E1A	SAE1	a	0.004
ubiquitin-like 1 (sentrin) activating enzyme E1B	UBA2	a	0.0011
UDP-Gal:betaGlc beta 1,3-galactosyltransferase, polypeptide 3	B3GALT3	a	0.0057
UDP-Gal:betaGlc beta 1,4- galactosyltransferase, polypeptide 2	B4GALT2	a	0.0005
UDP-N-acetyl-alpha-D-galactosamine:(N-acetylneuraminy)-galactosylglucosylceramide-beta-1, 4-N-acetylgalactosaminyltransferase	GALGT	*	0.0052
Unknown		*	0.0005
Unknown	ITGA5	*	0.0022
Unknown		*	0.0005
Unknown		*	0.0005
Unknown	COL18A1	(*)=*	0.0005; 0.0009
Unknown		*	0.006
Unknown		*	0.0012
Unknown		*	0.0096
Unknown		*	0.0191
Unknown		*	0.0367
Unknown		a	0.0424
Unknown		a	0.0047
Unknown		a	0.0019
Unknown		a	0.0005
Unknown		a	0.01
Unknown		a	0.0204
Unknown		a	0.0063
Unknown		a	0.0005
Unknown		a	0.0079
Unknown		a	0.0017
Unknown		a	0.0032
Unknown		a	0.0494
Unknown		a	0.0009
Unknown		a	0.0459

Unknown			a	0.0042			
Unknown			b				
Unknown			b				
Unknown			b				
Unknown			b				
Unknown			b				
Unknown			b				
Unknown			b				
Unknown			b				
Unknown			b				
upregulated during skeletal muscle growth 5	USMG5		b				
upstream transcription factor 1	USF1		a	0.01			
urokinase plasminogen activator receptor	PLAUR		*	0.0042			
UDP glycosyltransferase 1 family, polypeptide A6			b				
vascular cell adhesion molecule 1	VCAM1		b				
vascular endothelial growth factor A	VEGF		(a+b)=*	0.0219			
vascular endothelial zinc finger 1; expressed sequence A1848691	Vezf1		a	0.0305			
vasodilator-stimulated phosphoprotein	VASP		*	0.0054			
vitamin D receptor	VDR		a	0.0016			
v-ral simian leukemia viral oncogene homolog A (ras related)	RALA		b				
v-ral simian leukemia viral oncogene homolog B (ras related)	RALB		*	0.0005			
WD repeat domain 1	WDR1		a	0.0012			
Williams-Beuren syndrome chromosome region 14 homolog (human)	WBSCR14		a	0.0005			
WNT1 inducible sigling pathway protein 1	WISP1		b				
X (ictive)-specific transcript, antisense	TSIX		b				
X transporter protein 2	Xtup2		b				
Yamaguchi sarcoma viral (v-yes) oncogene homolog	YES1		b				
Yamaguchi sarcoma viral (v-yes-1) oncogene homolog	LYN		b				
yolk sac gene 2	DKFZp761A051.1		a	0.0046			
zinc finger like protein 1	ZFPL1		b				
zinc finger protein 144	ZNF144		b				
zinc finger protein 36, C3H type-like 1	ZFP36L1		*	0.0009			
zinc finger protein 36, C3H type-like 2	ZFP36L2		*	0.0005			
zotrin related factor 2	ZRF1		a	0.0118			
Gene name	fold (day 1-2 vs Normal-Ischemic)	p-value (day 5-14 vs Normal)	fold (day 5-14 vs Normal)	Expression of regeneration/normal : Early(A)/ Late(B)/ both (*) Vs. Normal; (Up (+); Down (-))	RCC/ normal kidney	RCC	Concordant (C) or Discordant (DC) with the renal regeneration dataset
(Gus-s) beta-glucuronidase structural		0.018	1.3665	(+)			
(Prlr-rs1) prolactin receptor related sequence 1	0.438069	0.009	0.5628	(-)			
(Sdcagg28) serologically defined colon cancer antigen 28	0.767583			(-)			



(AW146109) expressed sequence AW146109	1.762737	0.006	1.7551	(+)	(+)	C
(2610524K04Rik ; RIKEN cD 2610524K04 gene)	1.456446			(+)		
1-acylglycerol-3-phosphate O-acyltransferase 3 ; expressed sequence AW493985	0.741613			(-)	(-)	RCC C
2'-5' oligoadenylate synthetase 1A	1.224876			(+)		
2-hydroxyphytanoyl-CoA lyase		0.003	0.7615	(-)	(-)	RCC C
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1	0.711153			(-)		
3-phosphoglycerate dehydrogenase	1.523954			(+)	(-)/(+)	RCC conflict
4-hydroxyphenylpyruvic acid dioxygenase	0.305971	8E-04	0.3436	(-)	(-)	RCC C
5',3' nucleotidase, cytosolic		0.037	1.2614	(+)		
5-azacytidine induced gene 1	0.871679			(-)		
a disintegrin and metalloprotease domain 12 (meltrin alpha)	1.301018	0.018	1.2626	(+)		
a disintegrin-like and metalloprotease (repolysin type) with thrombospondin type 1 motif, 1	2.236459	8E-04	2.0162	(+)		
a disintegrin-like and metalloprotease (repolysin type) with thrombospondin type 1 motif, 2	1.226952			(+)		
A kinase (PRKA) anchor protein 2	1.477284			(+)	(-)	RCC DC
acetyl-Coenzyme A acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (D18Erd240e) RIKEN cD 0610011L04 gene	0.548469	0.002	0.5885	(-)		
acetyl-Coenzyme A dehydrogenase, medium chain	0.377562			(-)		
acetyl-Coenzyme A transporter	0.750342			(-)		
acidic ribosomal phosphoprotein PO	1.814377			(+)	(+)	RCC C
aconitase 1		0.009	0.7388	(-)	(-)	RCC C
actin related protein 2/3 complex, subunit 3 (21 kDa)	1.291043			(+)	(+)	RCC C
actin, alpha 1, skeletal muscle		0.022	1.7931	(+)		
actin, alpha 2, smooth muscle, aorta	2.549549	0.003	1.711	(+)		
actin, beta, cytoplasmic	1.861028	0.001	1.9517	(+)	(+)	RCC C
actin, gamma 2, smooth muscle, enteric	1.48389	0.008	1.7721	(+)		
actin-like	2.02784	0.036	1.7173	(+)		
activator of S phase kinase	1.418184			(+)		
activity-dependent neuroprotective protein		0.022	1.2684	(+)		
acyl-Coenzyme A dehydrogenase, short/branched chain	0.677684	0.009	0.7072	(-)	(-)	RCC C
acyl-Coenzyme A dehydrogenase, very long chain		0.005	0.7043	(-)		
acyl-Coenzyme A oxidase 1, palmitoyl		8E-04	0.4926	(-)	(+)	RCC DC
adaptor-related protein complex AP-3, sigma 1 subunit	1.221326			(+)	(+)	RCC C
adducin 3 (gamma)		0.008	0.7735	(-)	(+)	RCC DC
adenine phosphoribosyl transferase		0.044	1.3581	(+)		
adenylate cyclase 4	0.839219			(-)		

adenylate kinase 4	0.398031	8E-04	0.4203(-)			
adenylosuccinate synthetase 2, non muscle	1.307874	0.01	1.4121(+)			
adenylyl cyclase-associated CAP protein homolog 1 (S. cerevisiae, S. pombe)	1.526675		(+)			
ADP-ribosylation factor 1	1.301135		(+)			
ADP-ribosyltransferase (D+)	1.387701		(+)			
AE binding protein 1		0.035	1.4773(+)			
ajuba		0.004	1.2787(+)			
alcohol dehydrogenase 4 (class II), pi polypeptide		8E-04	0.5365(-)	(-)	RCCC	
aldehyde dehydrogenase family 1, subfamily A2		8E-04	1.6426(+)			
aldo-keto reductase family 1, member B8 ((Fgfrp) fibroblast growth factor regulated protein)	1.868794	0.004	1.534(+)			
aldo-keto reductase family 1, member C18 ; expressed sequence AW146047	0.403233		(-)			
alkaline phosphatase 2, liver	0.761972		(-)	(-)	RCCC	
ALL1-fused gene from chromosome 1q	0.820461		(-)			
alpha-methylacyl-CoA racemase	0.821375		(-)	(+)	RCCDC	
amelogenin		0.043	1.7776(+)			
amiloride binding protein 1 (amine oxidase, copper-containing)	1.636321	8E-04	3.1046(+)	(+)	RCCC	
amine N-sulfotransferase	0.581682		(-)			
aminoadipate-semialdehyde synthase/ (Lordsb) lysine oxoglutarate reductase, saccharopine dehydrogenase	0.505547	8E-04	0.4773(-)			
AMP deaminase 3		0.006	1.2946(+)			
annexin A1		8E-04	2.0545(+)	(+)/(???)	RCC conflict	
annexin A2	3.930545	8E-04	2.6506(+)	(-)/(+)	RCC conflict	
annexin A3		8E-04	2.1511(+)			
annexin A4		0.002	1.4492(+)	(+)	RCCC	
annexin A5	1.762505	8E-04	1.7547(+)			
annexin A6	1.403621	0.038	1.4849(+)			
anterior gradient 2 (Xenopus laevis)	0.74389		(-)			
apolipoprotein B editing complex 1		0.003	1.6053(+)			
apolipoprotein E		0.03	1.7135(+)	(-)	RCCDC	
apoptosis inhibitory protein 5		0.046	1.2954(+)			
apurinic/apyrimidinic endonuclease	1.513149		(+)			
aquaporin 2	0.604517		(-)			
arachidate 12-lipoxygenase, pseudogene 2		0.036	0.788(-)			
arachidate 5-lipoxygenase activating protein	1.299816		(+)	(+)	RCCC	
arginine-rich, mutated in early stage tumors	1.304171		(+)			
arginine type II		0.012	1.5597(+)			
Arpc2	1.6559	0.003	1.3245(+)			
ATP synthase, H+ transporting mitochondrial F1 complex, beta subunit	0.685294		(-)			

ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, alpha subunit, isoform 1	0.700665			(-)		
ATPase, +/K <sup>+</sup> transporting, beta 1 polypeptide		0.009	0.5031	(-)	(+)	RCCDC
ATPase, H <sup>+</sup> transporting, lysosomal (vacuolar proton pump), alpha 70 kDa, isoform 1	0.773098			(-)		
ATPase, H <sup>+</sup> transporting, V1 subunit F; RIKEN cD 1110004G16 gene	0.836034			(-)		
ATPase, H <sup>+</sup> /K <sup>+</sup> transporting, alpha polypeptide	0.786786			(-)		
ATP-binding cassette, sub-family A (ABC1), member 7		0.006	1.5416	(+)		
ATP-binding cassette, sub-family D (ALD), member 3	0.704394	8E-04	0.6847	(-)		
AU R binding protein/enoyl-coenzyme A hydratase	0.727287	0.022	0.7063	(-)		
avian reticuloendotheliosis viral (v-rel) oncogene related B		0.006	1.3329	(+)		
AXL receptor tyrosine kinase	1.476698	0.002	1.5274	(+)		
baculoviral IAP repeat-containing 1a	1.479547	8E-04	1.6192	(+)		
baculoviral IAP repeat-containing 2		0.003	1.5062	(+)	(+)	RCCC
baculoviral IAP repeat-containing 3		0.001	1.4791	(+)	(+)	RCCC
B-box and SPRY domain containing		0.002	1.3714	(+)		
B-cell leukemia/lymphoma 2 related protein A1b	1.425202	0.002	1.9462	(+)		
BCL2-antagonist/killer 1		0.04	1.2407	(+)		
Bcl-2-related ovarian killer protein		8E-04	1.6566	(+)		
benzodiazepine receptor, peripheral		0.003	1.5025	(+)		
beta-2 microglobulin		8E-04	2.3092	(+)	(+)	RCCC
betaine-homocysteine methyltransferase	0.463882			(-)	(-)	RCCC
biglycan	1.526097	8E-04	1.9267	(+)		
bisphosphate 3'-nucleotidase 1		0.003	0.6085	(-)		
Blu protein	0.711446			(-)		
bone marrow stromal cell antigen 1	1.303195	0.004	1.3219	(+)		
bone morphogenetic protein receptor, type 1A		0.01	1.2873	(+)		
brain protein 44-like	0.660344			(-)	(-)	RCCC
branched chain aminotransferase 2, mitochondrial	0.660946			(-)		
branched chain ketoacid dehydrogenase E1, alpha polypeptide	0.615398	8E-04	0.59	(-)	(+)	RCCDC
breakpoint cluster region protein 1	1.639424			(+)		
BRG1/brm-associated factor 53A	1.348562	0.015	1.4078	(+)		
Bromodomain and PHD finger containing, 3	0.78672			(-)		
cadherin 3	1.349831	8E-04	1.4592	(+)		
calbindin-28K	0.327595	0.014	0.4917	(-)	(-)	RCCC
calbindin-D9K	0.556398			(-)		
calcium channel, voltage-dependent, beta 3 subunit		0.038	1.4187	(+)	(+)	RCCC
calpain 2		0.001	1.2591	(+)		
calpain, small subunit 1	0.584314			(-)	(+)	RCCDC

calponin 2	1.384116	8E-04	1.8214(+)			
calreticulin	1.244306		(+)	(-)/(+)	RCC	conflict
calsyntenin 1	0.761543		(-)	(-)	RCC	C
capping protein beta 1	1.247283	0.023	1.4453(+)			
carbonic anhydrase 5a, mitochondrial	0.793202		(-)			
carboxylesterase 3	0.466372	0.008	0.5905(-)			
carboxypeptidase E		0.022	1.5977(+)			
carboxypeptidase X 1 (M14 family) / metallo-carboxypeptidase 1		0.011	1.4083(+)			
cardiac responsive adriamycin protein	1.578084		(+)			
carnitine palmitoyltransferase 1, liver	0.726551	0.002	0.5809(-)	(+)	RCC	DC
carnitine palmitoyltransferase 1, muscle	0.662861		(-)			
carnitine palmitoyltransferase 2	0.681572		(-)	(-)	RCC	C
cartilage oligomeric matrix protein	0.869318		(-)			
casein kse 1, epsilon		0.028	1.3466(+)			
caspase 1	0.75804		(-)	(+)(-)	RCC	conflict
caspase 3, apoptosis related cysteine protease		0.004	1.3961(+)			
caspase 8	1.169654		(+)			
cathepsin D	1.996407		(+)	(+)	RCC	C
cathepsin L	1.206119		(+)			
cathepsin S	1.733231	8E-04	4.4853(+)	(+)	RCC	C
cathepsin Z	1.23248		(+)			
Cbp/p300-interacting transactivator with Glu/Asp-rich carboxy-terminal domain 1		0.036	0.7565(-)			
CCCTC-binding factor	1.310333		(+)			
CD24a antigen	1.57732	8E-04	1.8903(+)	(+)	RCC	C
CD2-associated protein	1.4548	8E-04	1.766(+)	(+)	RCC	C
CD38 antigen	1.385877		(+)			
CD48 antigen		8E-04	1.8446(+)			
CD52 antigen		0.0008	2.63371; 2.413666	(+)	RCC	C
CD53 antigen	1.453756	0.004	1.5299(+)	(+)	RCC	C
CD59a antigen	0.783717		(-)	(+)	RCC	DC
CD68 antigen	1.767182	0.004	1.8367(+)	(+)	RCC	C
CD72 antigen	1.295352	0.003	1.5366(+)			
CDC16 (cell division cycle 16 homolog (S. cerevisiae))	1.191802		(+)	(+)	RCC	C
CDC28 protein kse 1	1.370272		(+)	(+)	RCC	C
CDK2 (cyclin-dependent kse 2)-associated protein 1	1.291944		(+)			
CEA-related cell adhesion molecule 1	0.670955	0.004	0.6695(-)	(+)	RCC	DC
CEA-related cell adhesion molecule 2	0.578039	0.014	0.6396(-)			
cell death-inducing D fragmentation factor, alpha subunit-like effector B	0.662515		(-)			
cell division cycle 2 homolog A (S. pombe)	1.989204		(+)			
cell division cycle 25 homolog A (S. cerevisiae)	1.164267		(+)			
cell division cycle 42 homolog (S. cerevisiae)	1.309167	0.002	1.5138(+)	(+)	RCC	C

cellular nucleic acid binding protein	1.26296		(+)	(+)	RCCC
centrin 2	0.850689		(-)		
centrin 3		0.032	1.2633(+)		
ceroid-lipofuscinosis, neuro1 2	0.766857		(-)		
chaperonin subunit 3 (gamma)	1.631384		(+)		
chemokine (C-C) receptor 2	1.379928	0.004	1.8554(+)	(+)	RCCC
chemokine (C-C) receptor 5	1.37154		(+)		
chemokine orphan receptor 1		8E-04	1.7518(+)		
chitinase 3-like 3	1.319784		(+)		
chloride channel calcium activated 1		0.02	1.325(+)		
chloride channel, nucleotide-sensitive, 1A		0.002	1.2654(+)		
chloride intracellular channel 1	2.425273	8E-04	1.9983(+)	(+)	RCCC
chloride intracellular channel 4 (mitochondrial)	1.319271	0.021	1.2476(+)		
cholinergic receptor, nicotinic, beta polypeptide 1 (muscle)		0.009	1.3002(+)		
citrate lyase beta like	0.749572		(-)		
clathrin, light polypeptide (Lca)	1.279741		(+)		
claudin 1	2.081215	0.001	1.5533(+)	(+)	RCCC
claudin 4	1.584524	0.005	1.6885(+)		
claudin 7	1.628062	8E-04	1.4804(+)		
cleavage and polyadenylation specific factor 5, 25 kD subunit		0.042	1.2755(+)		
clusterin	5.900022		(+)	(?)	RCC conflict
coagulation factor II (thrombin) receptor-like 1	1.422208	8E-04	1.3135(+)		
coagulation factor III	2.368334	0.003	1.7004(+)		
coagulation factor XIII, beta subunit	0.575972	8E-04	0.585(-)		
cofilin 1, non-muscle	2.223096		(+)	(+)(-)	RCC conflict
cold shock domain protein A	1.93466	9E-04	1.3519(+)	(+)	RCCC
colony stimulating factor 1 (macrophage)	1.711817		(+)	(+)	RCCC
complement component 1, q subcomponent, alpha polypeptide	1.61595	8E-04	2.7213(+)	(+)	RCCC
complement component 1, q subcomponent, beta polypeptide		8E-04	4.2321(+)	(+)	RCCC
complement component 1, q subcomponent, c polypeptide		8E-04	3.365(+)		
complement component 3	2.411628	8E-04	3.4754(+)		
complement component factor i	1.508817		(+)	(-)	RCCDC
complement factor H related protein 3A4/SG4		0.0009	2.204364(+)		
		0.0008	2.435881		
connective tissue growth factor		8E-04	1.6706(+)	(-)	RCCDC
constitutive photomorphogenic protein 1 (Arabidopsis)		0.019	1.276(+)		
coproporphyrinogen oxidase		0.001	0.6349(-)		
cordon-bleu ; ESTs, Moderately similar to T00381 KIAA0633 protein (H.sapiens)	1.27206		(+)		
core promoter element binding protein	1.534502; 1.708834	0.0148; 0.0008	1.622871; 2.094609	(+)	RCCC
cornichon homolog (Drosophila)	1.174252		(+)		
coronin, actin binding protein 1B	1.246811	0.022	1.4195(+)	(-)	RCCDC

craniofacial development protein 1	1.358741	0.004	1.3837	(+)			
creatine kinase, brain	0.625228			(-)			
cryptochrome 2 (photolyase-like)	0.75375			(-)			
crystallin, alpha B	1.724386			(+)	(+)	RCC C	
crystallin, lambda 1	0.682398	9E-04	0.6419	(-)			
crystallin, mu	1.739818	8E-04	2.9709	(+)	(-)	RCC DC	
cyclin E1	1.230927			(+)	(+)	RCC C	
cyclin-dependent kinase 4	1.709692			(+)			
cyclin-dependent kinase inhibitor 1A (P21)	1.764317			(+)	(+)/(+??)	RCC conflict	
cystatin B	2.140696	8E-04	1.98	(+)			
cystatin C		0.001	1.7744	(+)			
cysteine rich protein 61	2.006582	0.005	1.8544	(+)	(-)	RCC DC	
cytidine 5'-triphosphate synthase	1.458773	0.006	1.3569	(+)			
cytidine 5'-triphosphate synthase 2		0.002	1.2751	(+)			
cytochrome c oxidase, subunit VIc	0.738692			(-)	(+)	RCC DC	
cytochrome c oxidase, subunit VIIa 1	0.62639			(-)			
cytochrome c oxidase, subunit VIIa 3	0.755682			(-)			
cytochrome c oxidase, subunit VIIa		0.003	0.772	(-)			
cytochrome P450, 2a4	0.3663932; 0.4095392	0.005; 0.0089	0.5020061; 0.4404707	(-)			
cytochrome P450, 2d9	0.4799	8E-04	0.5423	(-)			
cytochrome P450, 2e1, ethanol inducible	0.63884			(-)			
cytochrome P450, 2j5	0.712681	0.016	0.7664	(-)			
cytochrome P450, family 4, subfamily v, polypeptide 3 / expressed sequence AW111961		0.014	1.5046	(+)			
cytochrome P450, subfamily IV B, polypeptide 1		0.002	0.4359	(-)			
cytokine inducible SH2-containing protein 3	2.296698	8E-04	2.0252	(+)			
D methyltransferase (cytosine-5) 1	1.45436			(+)			
D methyltransferase 3B	1.25679			(+)			
D primase, p49 subunit	1.356209			(+)			
D segment, Chr 12, ERATO Doi 604, expressed		0.025	1.3497	(+)			
D segment, Chr 17, ERATO Doi 441, expressed	1.385397	0.007	1.3747	(+)			
D segment, Chr 17, human D6S56E 2	1.274877			(+)			
D segment, Chr 18, Wayne State University 181, expressed	0.790825	0.037	0.6998	(-)	(-)	RCC C	
D segment, Chr 8, Brigham & Women's Genetics 1320 expressed	0.70845			(-)			
damage specific D binding protein 1 (127 kDa)	1.248195			(+)			
D-amino acid oxidase		0.044	0.7267	(-)			
D-dopachrome tautomerase	0.687173			(-)	(-)	RCC C	
DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 50 / nucleolar protein GU2		0.044	1.2423	(+)			
decorin		8E-04	1.6067	(+)	(-)	RCC DC	
deiodase, iodothyronine, type I	0.426139	0.004	0.5359	(-)			
deltex 1 homolog (Drosophila)	0.824274			(-)	(-)	RCC C	

deoxyribonuclease I	0.334306	8E-04	0.2485(-)			
diaphorase 1 (DH)	1.27042	0.03	1.3708(+)			
dihydropyrimidase	0.779607	0.002	0.7295(-)	(-)	RCCC	
dihydropyrimidase-like 3	1.24934		(+)	(+)	RCC C	
dimethylarginine		0.002	1.4038(+)			
dimethylaminohydrolase 2						
dipeptidase 1 (rel)	0.543074	0.003	0.5863(-)	(-)	RCCC	
DJ (Hsp40) homolog, subfamily A, member 1	0.696704		(-)			
DJ (Hsp40) homolog, subfamily B, member 12	0.805639		(-)			
DJ (Hsp40) homolog, subfamily C, member 5		0.022	1.2967(+)			
dolichyl-di-phosphooligosaccharide-protein glycotransferase	1.354829		(+)			
dopa decarboxylase	0.755528		(-)	(-)	RCCC	
double cortin and calcium/calmodulin-dependent protein kinase-like 1	1.267038		(+)			
downstream of tyrosine kinase 1		0.049	1.2419(+)			
DPH oxidase 4		0.002	0.5556(-)	(?)	RCC conflict	
E26 avian leukemia oncogene 2, 3' domain	1.244631		(+)			
E74-like factor 3	1.495613	8E-04	1.4218(+)	(+)	RCCC	
E74-like factor 4 (ets domain transcription factor)	1.355901	0.009	1.2619(+)			
early development regulator 2 (homolog of polyhomeotic 2)		0.004	1.4881(+)			
ectonucleoside triphosphate diphosphohydrolase 5	0.79518		(-)			
ectonucleotide	0.578313	8E-04	0.6047(-)	(+)	RCCDC	
pyrophosphatase/phosphodiesterase 2		8E-04	2.0862(+)			
EGF-like module containing, mucin-like, hormone receptor-like sequence 1						
EGL nine homolog 1 (C. elegans)	0.785405		(-)	(+)	RCCDC	
elafin-like protein I	0.289826		(-)			
elastase 1, pancreatic	0.579248		(-)			
elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 1	1.690045	8E-04	2.7756(+)			
endonuclease G	0.624758		(-)			
endoplasmic reticulum protein 29		0.028	1.384(+)			
endothelin 1	1.479734	8E-04	1.5711(+)			
enhancer of zeste homolog 2 (Drosophila)	1.357625		(+)			
enoyl Coenzyme A hydratase, short chain, 1, mitochondrial	0.728878		(-)			
epidermal growth factor	0.115294	8E-04	0.1981(-)	(-)	RCCC	
epidermal growth factor-containing fibulin-like extracellular matrix protein 1		0.002	1.4845(+)			
epidermal growth factor-containing fibulin-like extracellular matrix protein 2	1.736829	0.006	1.4624(+)			
epithelial membrane protein 3	1.838163	8E-04	1.4262(+)	(+)	RCCC	

erythrocyte protein band 4.1 / Mus musculus adult male tongue cD, RIKEN full-length enriched library, clone:2310065B16:erythrocyte protein band 4.1, full insert sequence		0.017	0.7166(-)	(-)	RCC	C
erythrocyte protein band 4.1-like 1	0.82105		(-)			
erythroid differentiation regulator	1.550627		(+)			
EST AI181838	0.72178		(-)			
estrogen related receptor, alpha	0.732545		(-)			
ESTs	0.735494	0.001	0.7011(-)			
ESTs	0.631426	0.035	0.697(-)			
ESTs	1.306482		(+)			
ESTs	0.772863		(-)			
ESTs	0.809355		(-)			
ESTs	1.345273		(+)			
ESTs	0.876828		(-)			
ESTs	1.357738		(+)			
ESTs	0.685626		(-)			
ESTs	0.804817		(-)			
ESTs	1.327383		(+)			
ESTs	0.498174		(-)			
ESTs	1.266278		(+)			
ESTs	0.755656		(-)			
ESTs	0.852094		(-)			
ESTs	0.844027		(-)			
ESTs	0.835016		(-)			
ESTs	1.316725		(+)			
ESTs	0.739721		(-)			
ESTs	0.733193		(-)			
ESTs	0.797542		(-)			
ESTs	0.855551		(-)			
ESTs	1.258533		(+)			
ESTs	0.810287		(-)			
ESTs	0.813422		(-)			
ESTs	0.788013		(-)			
ESTs	1.346671		(+)			
ESTs	1.30085		(+)			
ESTs		0.015	1.2779(+)			
ESTs		0.005	1.301(+)			
ESTs		0.003	1.5954(+)			
ESTs		8E-04	1.7006(+)			
ESTs		0.047	0.8025(-)			
ESTs		8E-04	1.582(+)			
ESTs		0.006	1.3173(+)			
ESTs		0.036	0.7972(-)			
ESTs		0.009	0.7379(-)			
ESTs		0.009	1.3453(+)			
ESTs		0.021	0.7619(-)			
ESTs		0.004	0.8135(-)			
ESTs		0.014	0.6346(-)			
ESTs		0.014	0.6812(-)			
ESTs -pending	1.272639		(+)			



ESTs, Highly similar to prefoldin 4 (Homo sapiens) (H.sapiens)	1.245303			(+)	(+)	RCC C
ESTs, Highly similar to organic cation transporter-like protein 2 (M.musculus)	0.728299			(-)		
ESTs, Highly similar to T00268 hypothetical protein KIAA0597 (H.sapiens)	0.736573			(-)		
ESTs, Moderately similar to SEC7 homolog (Homo sapiens) (H.sapiens)		0.005	0.6194	(-)		
ESTs, Moderately similar to S12207 hypothetical protein (M.musculus)	0.560434	0.004	0.6775	(-)		
ESTs, Moderately similar to T08673 hypothetical protein DKFZp564C0222.1 (H.sapiens)	0.733259	0.012	0.6844	(-)	(-)	RCC C
ESTs, Moderately similar to T46312 hypothetical protein DKFZp434J111.1 (H.sapiens)		0.005	1.4121	(+)		
ESTs, Weakly similar to brain-specific angiogenesis inhibitor 1-associated protein 2 (Mus musculus) (M.musculus)	0.743618			(-)		
ESTs, Weakly similar to limb expression 1 homolog (chicken) (Mus musculus) (M.musculus)	1.18303			(+)		
ESTs, Weakly similar to simple repeat sequence-containing transcript (Mus musculus) (M.musculus)		8E-04	1.2461	(+)		
ESTs, Weakly similar to 2022314A granule cell marker protein (M.musculus)		0.01	1.3354	(+)		
ESTs, Weakly similar to ADT1 MOUSE ADP,ATP CARRIER PROTEIN, HEART/SKELETAL MUSCLE ISOFORM T1 (M.musculus)	0.834522			(-)		
ESTs, Weakly similar to ADT1 MOUSE ADP,ATP CARRIER PROTEIN, HEART/SKELETAL MUSCLE ISOFORM T1 (M.musculus)	0.78616			(-)		
ESTs, Weakly similar to AF182426 1 arylacetamide deacetylase (R.norvegicus)	0.651341	8E-04	0.6067	(-)		
ESTs, Weakly similar to B Chain B, Crystal Structure Of Murine Soluble Epoxide Hydrolase Complexed With Cdu Inhibitor (M.musculus)		0.001	1.2499	(+)		
ESTs, Weakly similar to DRR1 (H.sapiens)	0.712178	0.015	0.7241	(-)		
ESTs, Weakly similar to JC7182 +- dependent vitamin C (H.sapiens)	0.840269			(-)		
ESTs, Weakly similar to JE0096 myocilin - mouse (M.musculus)		0.025	1.3969	(+)		
ESTs, Weakly similar to MAJOR URIRY PROTEIN 4 PRECURSOR (M.musculus)		0.03	0.8009	(-)		

ESTs, Weakly similar to S26689 hypothetical protein hc1 - mouse (M.musculus)	0.841829		(-)			
ESTs, Weakly similar to S65210 hypothetical protein YPL191c - yeast (Saccharomyces cerevisiae) (S.cerevisiae)	0.793096		(-)			
ESTs, Weakly similar to T29029 hypothetical protein F53G12.5 - Caenorhabditis elegans (C.elegans)	1.20938		(+)			
ESTs, Weakly similar to TS13 MOUSE TESTIS-SPECIFIC PROTEIN PBS13 (M.musculus)		0.008	1.2414(+)			
ESTs, Weakly similar to TYROSINE-PROTEIN KISE JAK3 (M.musculus)	0.70538	0.009	0.6835(-)			
ESTs, Weakly similar to TYROSINE-PROTEIN KISE JAK3 (M.musculus)	0.793884		(-)			
ESTs, Weakly similar to TYROSINE-PROTEIN KISE JAK3 (M.musculus)	1.330213		(+)			
ESTs, Weakly similar to YAE6 YEAST HYPOTHETICAL 13.4 KD PROTEIN IN ACS1-GCV3 INTERGENIC REGION (S.cerevisiae)	0.870445		(-)			
ESTs, Weakly similar to YMP2 CAEEL HYPOTHETICAL 30.3 KD PROTEIN B0361.2 IN CHROMOSOME III (C.elegans)	2.10875	0.004	1.8813(+)			
eukaryotic translation initiation factor 2A		0.005	1.294(+)			
eukaryotic translation initiation factor 3	1.274304		(+)			
eukaryotic translation initiation factor 3, subunit 4 (delta, 44 kDa)	1.340807		(+)	(+)	RCCC	
eukaryotic translation initiation factor 4, gamma 2	1.219128		(+)	(+)	RCCC	
eukaryotic translation initiation factor 4A1	1.342776	8E-04	1.506(+)	(+)	RCCC	
eukaryotic translation initiation factor 4A2	0.840329		(-)	(+)	RCCDC	
eukaryotic translation initiation factor 4E binding protein 1	1.627646	0.009	1.5179(+)			
eukaryotic translation initiation factor 5A	1.571166		(+)			
E-vasodilator stimulated phosphoprotein		0.044	1.316(+)	(+)	RCCC	
exportin 1, CRM1 homolog (yeast)	1.4997		(+)	(+)	RCCC	
expressed in non-metastatic cells 2, protein (NM23B) (nucleoside diphosphate kise)	1.329781		(+)	(+)	RCCC	
expressed sequence AA408783		0.005	1.5176(+)	(+)	RCCC	
expressed sequence AA589392	1.21524		(+)			
expressed sequence AA672638	0.777122		(-)			
expressed sequence AII117581	0.892163		(-)			
expressed sequence AII118577	0.739771	0.021	0.7424(-)			

expressed sequence AI132189	0.706946		(-)			
expressed sequence AI132321	1.342358	8E-04	2.4148(+)			
expressed sequence AI159688	0.465349	0.008	0.5963(-)			
expressed sequence AI182282	0.39936		(-)			
expressed sequence AI182284	0.610678	8E-04	0.5623(-)			
expressed sequence AI194696		8E-04	2.0538(+)			
expressed sequence AI265322	0.786084		(-)			
expressed sequence AI314027		0.003	1.3621(+)			
expressed sequence AI315037	0.873898		(-)			
expressed sequence AI316828		0.002	1.29(+)			
expressed sequence AI413331		0.022	1.2847(+)			
expressed sequence AI447451		8E-04	1.3615(+)			
expressed sequence AI448003		0.014	1.3551(+)			
expressed sequence AI449309		0.02	1.3528(+)			
expressed sequence AI450991	1.170481		(+)			
expressed sequence AI461788	1.143531		(+)			
expressed sequence AI465301	0.826408		(-)			
expressed sequence AI480660	0.819368		(-)			
expressed sequence AI504062	1.236201	0.008	1.3717(+)			
expressed sequence AI507121	0.674087		(-)			
expressed sequence AI528491	0.799738		(-)			
expressed sequence AI553555	0.731077		(-)			
expressed sequence AI558103	0.804878		(-)			
expressed sequence AI586180	1.401176	9E-04	1.3448(+)			
expressed sequence AI593249	0.503496	0.002	0.7107(-)			
expressed sequence AI593524		0.017	0.7462(-)			
expressed sequence AI604920		8E-04	1.433(+)			
expressed sequence AI607846	1.297307	0.003	1.5455(+)			
expressed sequence AI646725		0.046	0.7871(-)			
expressed sequence AI661919		0.006	0.8064(-)			
expressed sequence AI835705	0.63364		(-)			
expressed sequence AI836219	0.779958		(-)			
expressed sequence AI838057	0.711501		(-)			
expressed sequence AI843960		0.008	1.2221(+)			
expressed sequence AI844685	0.703625		(-)			
expressed sequence AI844876		0.003	0.7703(-)			
expressed sequence AI848669	0.925143		(-)			
expressed sequence AI852479	0.776527		(-)			
expressed sequence AI875199	0.768454		(-)			
expressed sequence AI875557	0.724579		(-)			
expressed sequence AI957255	0.692752		(-)			
expressed sequence AI987692		0.019	1.2573(+)			
expressed sequence AI.022757	1.770321		(+)			
expressed sequence AU015645	0.679211	0.011	0.6889(-)			
expressed sequence AU018056	0.813815		(-)			
expressed sequence AU019833		0.047	1.2608(+)			
expressed sequence AU042434		0.018	1.3037(+)			
expressed sequence AV046379	0.82172	0.027	0.7278(-)			
expressed sequence AW045860		0.038	0.8088(-)			
expressed sequence AW047581		0.031	1.3428(+)			
expressed sequence AW124722	0.803501		(-)			

WO 2006/083986

expressed sequence AW261723	0.668321	0.001	0.6447(-)		
expressed sequence AW413625	1.269501		(+)		
expressed sequence AW488255	0.877549		(-)		
expressed sequence AW493404		0.009	1.2209(+)		
expressed sequence AW541137		0.044	1.32(+)		
expressed sequence AW552393	0.890969		(-)		
expressed sequence AW743884		8E-04	2.0791(+)		
expressed sequence BB120430	1.229521		(+)		
expressed sequence C79732	0.742988		(-)		
expressed sequence C80913		0.029	1.1929(+)		
expressed sequence C81457		0.011	0.5924(-)		
expressed sequence C85317		0.007	1.3134(+)		
expressed sequence C85457	0.841033		(-)		
expressed sequence C86169	0.771679		(-)		
expressed sequence C86302	1.186345		(+)		
expressed sequence C87222	1.388445	0.005	1.3635(+)		
expressed sequence R75232	1.903157		(+)		
Fas apoptotic inhibitory molecule		0.001	1.3142(+)		
fatty acid synthase	0.487362		(-)		
f-box only protein 3	0.895328		(-)		
Fc receptor, IgE, high affinity I, gamma polypeptide	1.669993	8E-04	2.1723(+)	(+)	RCC C
Fc receptor, IgG, low affinity III	1.528608	9E-04	1.6917(+)	(+)	RCC C
feline sarcoma oncogene	1.220261		(+)	(+)	RCC C
fibrillarin	1.408148		(+)	(+)	RCC C
fibrillin 1	1.603484	0.009	1.583(+)		
fibulin 5	0.547159		(-)		
FK506 binding protein 10 (65 kDa)	1.569148		(+)		
FK506 binding protein 12-rapamycin associated protein 1	0.6659	0.014	0.7232(-)	(+)	RCC DC
FK506 binding protein 1a (12 kDa)	1.631333		(+)		
FK506 binding protein 5 (51 kDa)		8E-04	0.5428(-)		
FK506 binding protein 9	1.218167		(+)		
flap structure specific endonuclease 1	1.324505		(+)	(+)	RCC C
flavin containing monooxygenase 1	0.624819		(-)	(-)	RCC C
flotillin 1	1.818412		(+)		
flotillin 2	1.424145		(+)		
folate receptor 1 (adult)	0.654384	0.009	0.7132(-)	(-)/(+)	RCC conflict
forkhead box M1	1.42683		(+)		
four and a half LIM domains 1		0.007	0.736(-)	(+)	RCC DC
fragile histidine triad gene	1.305838		(+)	(-)	RCC DC
fumarylacetoacetate hydrolase	0.554798	8E-04	0.5524(-)	(-)	RCC C
FXD domain-containing ion transport regulator 2		0.008	0.6338(-)	(-)	RCC C
FXD domain-containing ion transport regulator 5	1.873781	8E-04	1.5927(+)		
G protein-coupled receptor kise 7	0.743286		(-)	(+)	RCC DC
G1 to phase transition 1	1.490601		(+)		
gamma-glutamyl hydrolase		0.013	1.2696(+)	(+)(-)	RCC conflict

gamma-glutamyl transpeptidase	0.562559	8E-04	0.5141(-)			
ganglioside-induced differentiation-associated-protein 3		0.029	1.262(+)			
gap junction membrane channel protein beta 2		0.034	0.6818(-)	(+)	RCC	DC
glucose regulated protein, 58 kDa	1.334846		(+)	(+)	RCC	C
glucose-6-phosphatase, catalytic	0.331086	8E-04	0.3315(-)			
glucose-6-phosphatase, transport protein 1	0.504687		(-)			
glutamine synthetase	0.506746	8E-04	0.3378(-)			
glutaryl-Coenzyme A dehydrogenase	0.620166	8E-04	0.5593(-)			
glutathione peroxidase 1	1.376036		(+)	(+)	RCC	C
glutathione S-transferase, alpha 2 (Yc2)		0.01	0.6945(-)	(+)(-)	RCC	conflict
glutathione S-transferase, alpha 4		0.028	0.6627(-)			
glutathione S-transferase, mu 6	1.475521		(+)			
glutathione S-transferase, pi 1	1.385566		(+)			
glutathione S-transferase, theta 2	0.636317		(-)	(-)	RCC	C
glutathione transferase zeta 1 (maleylacetoacetate isomerase)	0.634449		(-)			
glycerol kase	0.520913	0.002	0.5752(-)	(-)	RCC	C
glycerol phosphate dehydrogenase 1, mitochondrial		0.004	0.6803(-)			
glycerol-3-phosphate acyltransferase, mitochondrial	0.66301	0.002	0.7084(-)			
glycine amidinotransferase (L-arginine:glycine amidinotransferase)	0.543395	0.003	0.6865(-)	(-)	RCC	C
glycine N-methyltransferase	0.580827		(-)			
glycoprotein 49 A	1.8182	0.002	1.8947(+)			
glycoprotein 49 B	1.831723	0.013	1.6056(+)			
glypican 3		8E-04	2.3509(+)	(-)	RCC	DC
golgi autoantigen, golgin subfamily a, 4	0.744408		(-)			
golgi reassembly stacking protein 2	1.172165	0.007	1.291(+)	(+)	RCC	C
GPI-anchored membrane protein 1	1.309942		(+)	(+)	RCC	C
granulin	1.290686		(+)	(+)	RCC	C
G-rich RNA sequence binding factor 1 (D5Wsu31e) D segment, Chr 5, Wayne State University 31, expressed		0.028	0.7285(-)	(+)	RCC	DC
group specific component	1.498652		(+)	(-)	RCC	DC
growth arrest and D-damage-inducible 45 alpha	1.493038	0.002	1.6622(+)			
growth arrest and D-damage-inducible 45 gamma		0.001	0.4592(-)	(+)	RCC	DC
growth arrest specific 2	0.632398	8E-04	0.6609(-)	(-)	RCC	C
growth differentiation factor 15	1.635441	0.045	1.5152(+)	(+)	RCC	C
growth differentiation factor 8		0.001	1.3728(+)			
growth factor receptor bound protein 7	0.798278		(-)	(-)	RCC	C
guanine nucleotide binding protein (G protein), gamma 2 subunit		0.022	1.316(+)			
guanine nucleotide binding protein (G protein), gamma 5 subunit	0.497877	0.001	0.5933(-)			
guanine nucleotide binding protein, alpha inhibiting 2	1.428688	0.005	1.6772(+)	(+)	RCC	C

guanine nucleotide binding protein, beta 2, related sequence 1	1.942687	0.001	1.4495(+)	(+)	RCC C
guanosine diphosphate (GDP) dissociation inhibitor 3	1.194521		(+)		
guanosine monophosphate reductase	1.409698	0.042	1.4131(+)		
guanylate nucleotide binding protein 2		8E-04	1.83(+)	(+)	RCC C
H2A histone family, member Z	1.937214	0.025	1.5002(+)	(+)	RCC C
H2B histone family, member S	0.757011		(-)		
Harvey rat sarcoma oncogene, subgroup R	1.512845		(+)		
heat shock 70 kDa protein 4	1.296849; 1.316802		(+)		
heat shock protein 1 (chaperonin) / heat shock protein, 60 kDa		9E-04	0.6689(-)	(+)	RCC DC
heat shock protein, 105 kDa		0.015	0.729(-)	(+)	RCC DC
heat shock protein, 86 kDa 1	1.645544		(+)	(?)	RCC conflict
heat-responsive protein 12	0.647694		(-)	(-)	RCC C
hematological and neurological expressed sequence 1	1.563803		(+)	(+)	RCC C
heme oxygenase (decycling) 1	1.922685		(+)		
hemochromatosis		0.001	1.2616(+)		
hemopoietic cell phosphatase	1.582381	9E-04	1.5358(+)	(+)	RCC C
heparan sulfate 2-O-sulfotransferase 1	1.173811		(+)		
heparin binding epidermal growth factor-like growth factor	1.358949		(+)		
hepatic nuclear factor 4		8E-04	0.6498(-)		
hepatoma-derived growth factor	1.180861		(+)		
hepsin	0.761344	0.036	0.7761(-)	(-)	RCC C
heterogeneous nuclear ribonucleoprotein A1	2.419538	8E-04	1.8593(+)	(+)	RCC C
hexokise 1	0.766611		(-)	(+)	RCC DC
high mobility group AT-hook 1	2.462143		(+)		
high mobility group box 3	1.355483	0.002	1.564(+)	(+)	RCC C
high mobility group nucleosomal binding domain 2	1.760107	0.018	1.2532(+)	(+)	RCC C
histidyl tR synthetase	0.708007		(-)	(+)	RCC DC
histocompatibility 2, class II antigen A, alpha		8E-04	4.0415(+)		
histocompatibility 2, class II antigen E beta		8E-04	2.9829(+)		
histocompatibility 2, class II, locus DMa		0.002	1.7963(+)		
Histocompatibility 2, D region locus 1	1.483204	8E-04	1.9955(+)		
histocompatibility 2, Q region locus 7		0.005	1.6855(+)		
histone 2, H2aa1 / (Hist2) histone gene complex 2		0.026	0.7303(-)		
histone deacetylase 1		0.012	1.4367(+)		
homeo box B7	1.189729		(+)		

homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	0.52813	8E-04	0.4351(-)			
Hoxc8	1.638671		(+)			
Hprt	1.377124		(+)			
hyaluron mediated motility receptor (RHAMM)	1.236898		(+)			
hyaluronic acid binding protein 2		0.044	0.7814(-)			
hydroxysteroid 17-beta dehydrogenase 7		0.014	0.7563(-)			
hydroxysteroid dehydrogenase-1, delta<5>-3-beta	0.537309		(-)			
hydroxysteroid dehydrogenase-3, delta<5>-3-beta	0.57926		(-)			
hypothetical protein, I54	0.496484	9E-04	0.5491(-)			
hypothetical protein, MGC:6957		0.024	1.3597(+)			
hypothetical protein, MNCB-5210		0.004	1.5476(+)			
Ia-associated invariant chain		8E-04	4.38(+)	(+)	RCCC	
immunoglobulin superfamily, member 8	1.150677		(+)			
importin 11 (RIKEN cDNA 2510001A17 gene)	1.293414		(+)			
inhibin beta-B	1.257506		(+)	(+)	RCCC	
inhibitor of D binding 2		8E-04	1.4816(+)	(+)	RCCC	
inosine 5'-phosphate dehydrogenase 2	1.550038		(+)			
inositol polyphosphate-5-phosphatase, 75 kDa	0.700199	0.037	0.7627(-)			
insulin-like growth factor binding protein 1	0.682742		(-)	(+)	RCCDC	
insulin-like growth factor binding protein 3	0.558403		(-)	(+)	RCCDC	
insulin-like growth factor binding protein 4	0.574239		(-)			
insulin-like growth factor binding protein, acid labile subunit	0.738802		(-)			
integrin alpha 6		0.03	1.4584(+)	(+)	RCCC	
integrin alpha M	1.291467		(+)	(+)	RCCC	
integrin beta 1 (fibronectin receptor beta)		8E-04	1.5674(+)	(+)	RCCC	
integrin-associated protein		0.019	1.4362(+)	(+/?)	RCC conflict	
intercellular adhesion molecule	1.556701	0.021	1.5598(+)	(+)	RCCC	
interferon activated gene 204		0.0014; 0.0038	1.686958; 1.556905	(+)		
interferon gamma receptor		0.006	1.497(+)	(+)	RCCC	
interferon inducible protein 1	0.707584		(-)			
interferon-induced protein with tetratricopeptide repeats 3	1.847808		(+)			
integral membrane protein 1	1.321916		(+)			
interleukin 1 beta	1.536653		(+)	(?)	RCC conflict	
interleukin 1 receptor, type I	1.304397		(+)			
interleukin 11 receptor, alpha chain 1	0.723197		(-)			
isocitrate dehydrogenase 2 (DP+), mitochondrial	0.756124	0.003	0.7726(-)			

isovaleryl coenzyme A dehydrogese	0.6145993; 0.5060046	0.004	0.6321(-)			
J domain protein 1	0.583849	0.005	0.5726(-)			
junction plakoglobin	0.554028		(-)	(-)	RCCC	
kallikrein 26	0.573494	0.029	0.6276(-)			
kallikrein 6	0.625692	8E-04	0.5089(-)	(+)	RCCDC	
karyopherin (importin) alpha 2	1.591718		(+)	(+)	RCCC	
karyopherin (importin) beta 3	1.334861		(+)			
keratin complex 1, acidic, gene 19		0.041	1.5647(+)	(+)	RCCC	
keratin complex 2, basic, gene 8	3.335629	8E-04	2.1229(+)	(+)	RCCC	
ketohekoise	0.408655	0.018	0.629(-)	(-)	RCCC	
kidney-derived aspartic protease-like protein	0.351128	8E-04	0.4507(-)			
kinecin 1		0.003	1.3275(+)			
kinesin family member 1B (expressed sequence A1448212)	1.155435		(+)			
kinesin family member 21A	0.854366		(-)	(+)	RCCDC	
kise insert domain protein receptor	0.839918		(-)	(+)	RCCDC	
klotho	0.469163	8E-04	0.5128(-)	(-)	RCCC	
Kruppel-like factor 1 (erythroid)	0.688283		(-)			
Kruppel-like factor 15	0.438157	8E-04	0.5538(-)			
Kruppel-like factor 5	1.315458		(+)	(+)	RCCC	
Kruppel-like factor 9	0.582456	8E-04	0.5909(-)			
kynureninase (L-kynurenine hydrolase)	0.745856		(-)			
L-3-hydroxyacyl-Coenzyme A dehydrogese, short chain	0.718971	0.004	0.6765(-)	(-)	RCCC	
lactate dehydrogese 1, A chain	1.323347		(+)	(+)	RCCC	
laminin B1 subunit 1	1.342184		(+)			
laminin receptor 1 (67kD, ribosomal protein SA)	1.663287	0.003	1.7401(+)	(+)	RCCC	
laminin, alpha 2		0.005	1.3048(+)	(+)	RCCC	
latexin	1.246623		(+)	(+)	RCCC	
lectin, galactose binding, soluble 3	3.883012	8E-04	2.5131(+)	(+)	RCCC	
lectin, galactose binding, soluble 4	0.732914		(-)			
lectin, galactose binding, soluble 9	1.21399		(+)	(+)/(- ???)	RCCconflict	
leucine zipper-EF-hand containing transmembrane protein 1	0.740398	0.012	0.7633(-)			
leucocyte specific transcript 1		0.012	1.3889(+)	(+)	RCCC	
leukemia-associated gene	2.2171		(+)	(+)	RCCC	
leukotriene C4 synthase	1.287439		(+)			
LIM and SH3 protein 1		0.004	1.5453(+)			
lipoprotein lipase	0.361706	0.001	0.5653(-)	(+)	RCCDC	
liver-specific bHLH-Zip transcription factor		0.004	1.3774(+)			
low density lipoprotein receptor-related protein 2	0.546832		(-)	(-)	RCCC	
low density lipoprotein receptor-related protein 6	0.759073		(-)			
LPS-induced TNF-alpha factor	2.017366	8E-04	1.7774(+)			
lymphocyte antigen 6 complex, locus A	1.627074		(+)			



lymphocyte antigen 6 complex, locus E	1.99767	8E-04	2.5458(+)			
lymphocyte specific 1	1.322083	0.003	2.0054(+)	(+)	RCC	C
lyric (D8Bwg1112e) D segment, Chr 8, Brigham & Women's Genetics 1112 expressed		0.048	1.2049(+)			
lysosomal-associated protein transmembrane 4A		0.025	1.2854(+)			
lysosomal-associated protein transmembrane 4B		8E-04	1.2595(+)			
lysosomal-associated protein transmembrane 5		0.017	2.1031(+)	(+)	RCC	C
lysozyme		8E-04	5.7532(+)	(+)	RCC	C
lysyl oxidase-like	1.390075		(+)			
M.musculus mR for protein expressed at high levels in testis		0.032	0.7977(-)			
macrophage expressed gene 1	1.484724	8E-04	2.774(+)			
macrophage migration inhibitory factor		0.015	0.674(-)			
macrophage scavenger receptor 2		8E-04	1.7086(+)			
MAD homolog 5 (Drosophila) / expressed sequence A1451355		0.008	1.3266(+)	(+)	RCC	C
mago-shi homolog, proliferation-associated (Drosophila)	1.277107		(+)	(+)	RCC	C
major vault protein	1.428351		(+)			
malate dehydrogenase, soluble	0.581342	8E-04	0.6478(-)			
malic enzyme, supertant	0.683208	0.006	0.7935(-)			
malonyl-CoA decarboxylase	0.635893	0.001	0.718(-)			
mammary tumor integration site 6	1.358134	0.009	1.3053(+)	(+)	RCC	C
mannose receptor, C type 1		8E-04	1.738(+)			
mannose-6-phosphate receptor, cation dependent		0.025	1.3348(+)			
MARCKS-like protein		8E-04	1.8277(+)			
matrix gamma-carboxylglutamate (gla) protein	2.076147	8E-04	6.6453(+)			
matrix metalloproteinase 14 (membrane-inserted)		8E-04	2.0556(+)	(+)	RCC	C
matrix metalloproteinase 2		0.002	1.5675(+)	(-)	RCC	DC
matrix metalloproteinase 23		0.019	1.2949(+)			
matrix metalloproteinase 7		0.014	1.921(+)	(+)	RCC	C
max binding protein		0.024	1.2911(+)			
melanoma antigen, family D, 2	1.25115	8E-04	1.3993(+)			
meprin 1 alpha	0.603084	0.026	0.7488(-)	(+)	RCC	DC
metallothionein 1	1.799613	0.003	0.7041(+)			
metallothionein 2	2.336497		(+)	(-)	RCC	DC
metastasis associated 1-like 1		0.013	1.3714(+)			
methionine aminopeptidase 2	1.198553		(+)			
methyl CpG binding protein 2		0.011	0.8021(-)			
methylene tetrahydrofolate dehydrogenase (DP+ dependent), methenyl tetrahydrofolate cyclohydrolase,	0.655893	0.004	0.6176(-)	(+)	RCC	DC

formyltetrahydrofolate synthase							
methylmalonyl-Coenzyme A mutase	0.696844	0.042	0.7871	(-)			
microfibrillar associated protein 5		8E-04	1.4456	(+)			
microtubule associated testis specific serine/threonine protein kise	1.211841			(+)			
microtubule-associated protein tau	0.669051			(-)			
microtubule-associated protein, RP/EB family, member 1	1.295375			(+)			
mini chromosome maintenance deficient (S. cerevisiae)	1.767788			(+)	(+)	RCCC	
mini chromosome maintenance deficient 2 (S. cerevisiae)	1.400229			(+)	(+)	RCCC	
mini chromosome maintenance deficient 4 homolog (S. cerevisiae)	1.61344			(+)	(+)	RCCC	
mini chromosome maintenance deficient 7 (S. cerevisiae)	1.676881			(+)	(+)	RCCC	
mitochondrial ribosomal protein L39	0.61503			(-)			
mitochondrial ribosomal protein L50; (D4Wsu125e) D segment, Chr 4, Wayne State University 125, expressed	0.844369			(-)			
Mitogen activated protein kinase 1 ; RIKEN cD 9030612K14 gene	0.881133			(-)			
mitogen activated protein kise 13	1.284772			(+)			
mitogen activated protein kise kise kise 1	1.44774			(+)			
mitogen-activated protein kise 7	1.154393			(+)			
mitsugumin 29	0.746943			(-)			
MORF-related gene X	1.75411			(+)	(+)	RCCC	
Mufl protein (D630045E04Rik) Mus musculus, clone IMAGE:3491421, mR, partial cds		0.029	1.3063	(+)			
Mus musculus adult male kidney cD, RIKEN full-length enriched library, clone:0610012C11:homogenisate 1, 2-dioxygese, full insert sequence	0.83441			(-)			
Mus musculus adult male liver cD, RIKEN full-length enriched library, clone:1300015E02:deoxyribonuclease II alpha, full insert sequence	0.497964			(-)			
Mus musculus chemokine receptor CCX CKR mR, complete cds, alternatively spliced	0.684535	0.005	0.748	(-)			
Mus musculus evectin-2 (Evt2) mR, complete cds	0.708842			(-)			
Mus musculus LDLR dan mR, complete cds	0.768717			(-)			
Mus musculus mR for 67 kDa polymerase-associated factor PAF67 (paf67 gene)	1.237055			(+)			
Mus musculus mR for alpha-albumin protein	0.602557			(-)	(-)	RCCC	

Mus musculus, basic transcription factor 3, clone MGC:6799 IMAGE:2648048, mR, complete cds	1.560713			(+)			
Mus musculus, clone IMAGE:3155544, mR, partial cds	0.81178			(-)			
Mus musculus, clone IMAGE:3494258, mR, partial cds	1.496563	0.002	1.4937	(+)			
Mus musculus, clone IMAGE:3586777, mR, partial cds	0.757009	0.043	0.7969	(-)			
Mus musculus, clone IMAGE:3589087, mR, partial cds	0.627399			(-)			
Mus musculus, clone IMAGE:3967158, mR, partial cds	0.81385			(-)			
Mus musculus, clone IMAGE:3994696, mR, partial cds		8E-04	1.6172	(+)			
Mus musculus, clone IMAGE:4456744, mR, partial cds	1.225829			(+)			
Mus musculus, clone IMAGE:4486265, mR, partial cds	1.530214			(+)			
Mus musculus, clone IMAGE:4952483, mR, partial cds		8E-04	2.1916	(+)			
Mus musculus, clone IMAGE:4974221, mR, partial cds	0.695028			(-)	(-)	RCCC	
Mus musculus, clone MGC:12039 IMAGE:3603661, mR, complete cds	0.824624			(-)			
Mus musculus, clone MGC:12159 IMAGE:3711169, mR, complete cds		0.014	1.3329	(+)			
Mus musculus, clone MGC:18871 IMAGE:4234793, mR, complete cds		0.0103; 0.0305	0.6239812; 0.7169	(-)	(-)	RCCC	
Mus musculus, clone MGC:18985 IMAGE:4011674, mR, complete cds	1.364034			(+)	(+)	RCCC	
Mus musculus, clone MGC:19042 IMAGE:4188988, mR, complete cds	0.675484			(-)			
Mus musculus, clone MGC:19361 IMAGE:4242170, mR, complete cds	1.245176			(+)			
Mus musculus, clone MGC:29021 IMAGE:3495957, mR, complete cds	1.50073			(+)			
Mus musculus, clone MGC:36388 IMAGE:5098924, mR, complete cds	0.545973	0.006	0.6647	(-)			
Mus musculus, clone MGC:36554 IMAGE:4954874, mR, complete cds		0.02	1.3223	(+)			
Mus musculus, clone MGC:36997 IMAGE:4948448, mR, complete cds	1.181755			(+)			
Mus musculus, clone MGC:37818 IMAGE:5098655, mR, complete cds	0.605546	0.022	0.6467	(-)			
Mus musculus, clone MGC:38363 IMAGE:5344986, mR, complete cds		8E-04	1.5819	(+)	(-)	RCCDC	
Mus musculus, clone MGC:38798 IMAGE:5359803, mR, complete cds	0.804721			(-)			
Mus musculus, clone MGC:6377 IMAGE:3499365, mR, complete cds	1.153319			(+)			
Mus musculus, clone MGC:6545 IMAGE:2655444, mR, complete cds	0.719589			(-)	(+)	RCCDC	
Mus musculus, clone MGC:7898 IMAGE:3582717, mR, complete cds	0.640881	0.008	0.6501	(-)			

10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 313 314 315 316 317 318 319 320 321 322 323 324 325 326 327 328 329 330 331 332 333 334 335 336 337 338 339 340 341 342 343 344 345 346 347 348 349 350 351 352 353 354 355 356 357 358 359 360 361 362 363 364 365 366 367 368 369 370 371 372 373 374 375 376 377 378 379 380 381 382 383 384 385 386 387 388 389 390 391 392 393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 471 472 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 491 492 493 494 495 496 497 498 499 500 501 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517 518 519 520 521 522 523 524 525 526 527 528 529 530 531 532 533 534 535 536 537 538 539 540 541 542 543 544 545 546 547 548 549 550 551 552 553 554 555 556 557 558 559 560 561 562 563 564 565 566 567 568 569 570 571 572 573 574 575 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 595 596 597 598 599 600 601 602 603 604 605 606 607 608 609 610 611 612 613 614 615 616 617 618 619 620 621 622 623 624 625 626 627 628 629 630 631 632 633 634 635 636 637 638 639 640 641 642 643 644 645 646 647 648 649 650 651 652 653 654 655 656 657 658 659 660 661 662 663 664 665 666 667 668 669 670 671 672 673 674 675 676 677 678 679 680 681 682 683 684 685 686 687 688 689 690 691 692 693 694 695 696 697 698 699 700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716 717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732 733 734 735 736 737 738 739 740 741 742 743 744 745 746 747 748 749 750 751 752 753 754 755 756 757 758 759 760 761 762 763 764 765 766 767 768 769 770 771 772 773 774 775 776 777 778 779 780 781 782 783 784 785 786 787 788 789 790 791 792 793 794 795 796 797 798 799 800 801 802 803 804 805 806 807 808 809 810 811 812 813 814 815 816 817 818 819 820 821 822 823 824 825 826 827 828 829 830 831 832 833 834 835 836 837 838 839 840 841 842 843 844 845 846 847 848 849 850 851 852 853 854 855 856 857 858 859 860 861 862 863 864 865 866 867 868 869 870 871 872 873 874 875 876 877 878 879 880 881 882 883 884 885 886 887 888 889 890 891 892 893 894 895 896 897 898 899 900 901 902 903 904 905 906 907 908 909 910 911 912 913 914 915 916 917 918 919 920 921 922 923 924 925 926 927 928 929 930 931 932 933 934 935 936 937 938 939 940 941 942 943 944 945 946 947 948 949 950 951 952 953 954 955 956 957 958 959 960 961 962 963 964 965 966 967 968 969 970 971 972 973 974 975 976 977 978 979 980 981 982 983 984 985 986 987 988 989 990 991 992 993 994 995 996 997 998 999 1000

Mus musculus, hypothetical protein MGC11287 similar to ribosomal protein S6 kise, clone MGC:28043 IMAGE:3672127, mR, complete cds	0.834745			(-)				
Mus musculus, Similar to 60S ribosomal protein L30 isolog, clone MGC:6735 IMAGE:3590401, mR, complete cds	0.854772			(-)				
Mus musculus, Similar to angiotensin-like factor, clone MGC:32448 IMAGE:5043159, mR, complete cds		0.036	0.7253	(-)				
Mus musculus, Similar to CGI-147 protein, clone MGC:25743 IMAGE:3990061, mR, complete cds	1.221941	0.019	1.2422	(+)				
Mus musculus, Similar to chromosome 20 open reading frame 36, clone IMAGE:5356821, mR, partial cds	0.783228	0.007	0.8377	(-)				
Mus musculus, Similar to cortactin isoform B, clone MGC:18474 IMAGE:3981559, mR, complete cds	1.340479			(+)				
Mus musculus, Similar to dendritic cell protein, clone MGC:11741 IMAGE:3969335, mR, complete cds	1.385299	0.046	1.3457	(+)				
Mus musculus, Similar to DKFZP586B0621 protein, clone MGC:38635 IMAGE:5355789, mR, complete cds		8E-04	1.8677	(+)				
Mus musculus, similar to heterogeneous nuclear ribonucleoprotein A3 (H. sapiens), clone MGC:37309 IMAGE:4975085, mR, complete cds	1.739406	0.01	1.3073	(+)				
Mus musculus, Similar to hypothetical protein DKFZp566A1524, clone MGC:18989 IMAGE:4012217, mR, complete cds	1.338865			(+)				
Mus musculus, Similar to hypothetical protein FLJ10520, clone MGC:27888 IMAGE:3497792, mR, complete cds	0.533357			(-)				
Mus musculus, Similar to hypothetical protein FLJ12618, clone MGC:28775 IMAGE:4487011, mR, complete cds	0.750638			(-)				
Mus musculus, Similar to hypothetical protein FLJ13213, clone MGC:28555 IMAGE:4206928, mR, complete cds	1.108571			(+)				
Mus musculus, Similar to hypothetical protein FLJ20234, clone MGC:37525 IMAGE:4986113, mR, complete cds		8E-04	1.759	(+)				
Mus musculus, Similar to hypothetical protein FLJ20245, clone MGC:7940 IMAGE:3584061, mR, complete cds		0.003	1.2319	(+)				

Mus musculus, Similar to hypothetical protein FLJ20335, clone MGC:28912 IMAGE:4922274, mR, complete cds	1.400228			(+)			
Mus musculus, Similar to hypothetical protein FLJ21634, clone MGC:19374 IMAGE:2631696, mR, complete cds	0.475177	0.036	0.6585	(-)			
Mus musculus, Similar to hypothetical protein MGC3133, clone MGC:11596 IMAGE:3965951, mR, complete cds	1.337296			(+)			
Mus musculus, Similar to hypothetical protein MGC4368, clone MGC:28978 IMAGE:4503381, mR, complete cds		0.004	0.7732	(-)			
Mus musculus, Similar to KIAA0763 gene product, clone IMAGE:4503056, mR, partial cds	0.804691			(-)			
Mus musculus, Similar to KIAA1075 protein, clone IMAGE:5099327, mR, partial cds	0.648409	8E-04	0.6346	(-)			
Mus musculus, Similar to MIPP65 protein, clone MGC:18783 IMAGE:4188234, mR, complete cds	0.720364			(-)			
Mus musculus, Similar to nucleolar cysteine-rich protein, clone MGC:6718 IMAGE:3586161, mR, complete cds --pending		0.001	1.3895	(+)	(+)	RCCC	
Mus musculus, Similar to Protein P3, clone MGC:38638 IMAGE:5355849, mR, complete cds		0.003	1.2526	(+)			
Mus musculus, similar to quinone reductase-like protein, clone IMAGE:4972406, mR, partial cds	0.5749			(-)			
Mus musculus, similar to R29893_1, clone MGC:37808 IMAGE:5098192, mR, complete cds	0.716169			(-)			
Mus musculus, Similar to RAS p21 protein activator, clone MGC:7759 IMAGE:3498774, mR, complete cds	1.176812			(+)			
Mus musculus, Similar to retinol dehydrogenase type 6, clone MGC:25965 IMAGE:4239862, mR, complete cds	0.48924			(-)			
Mus musculus, Similar to ribosomal protein S20, clone MGC:6876 IMAGE:2651405, mR, complete cds		8E-04	1.6264	(+)			
Mus musculus, Similar to sirtuin silent mating type information regulation 2 homolog 7 (S. cerevisiae), clone MGC:37560 IMAGE:4987746, mR, complete cds	0.828673			(-)			
Mus musculus, Similar to transgelin 2, clone MGC:6300 IMAGE:2654381, mR, complete cds	2.078132	8E-04	1.8563	(+)	(+)	RCCC	
Mus musculus, Similar to ubiquitin-conjugating enzyme E2 variant 1, clone MGC:7660 IMAGE:3496088,	0.669748	8E-04	0.6707	(-)	(+)	RCCDC	

mR, complete cds						
Mus musculus, Similar to unc93 (C.elegans) homolog B, clone MGC:25627 IMAGE:4209296, mR, complete cds		8E-04	2.1075	(+)		
Mus musculus, Similar to xylulokise homolog (H. influenzae), clone IMAGE:5043428, mR, partial cds	0.63543	0.023	0.6757	(-)		
mutS homolog 2 (E. coli)	1.173315			(+)	(+)	RCCC
mutS homolog 6 (E. coli)	1.287113			(+)		
MYB binding protein (P160) 1a	1.37183			(+)		
MYC-associated zinc finger protein (purine-binding transcription factor)	1.330611			(+)	(+)	RCCC
myelocytomatosis oncogene	1.459356	0.014	1.4883	(+)	(+)	RCCC
myeloid differentiation primary response gene 88		0.004	1.441	(+)		
myeloid-associated differentiation marker	1.390891			(+)		
myocyte enhancer factor 2A		0.009	1.2539	(+)	(+)(-)	RCC conflict
myosin Ic	1.288644			(+)		
myosin light chain, alkali, cardiac atria	1.622514			(+)		
myosin light chain, alkali, nonmuscle		0.028	1.4658	(+)	(-)	RCCDC
myristoylated alanine rich protein kase C substrate		8E-04	1.8458	(+)		
N-acetylglucosamine kase	1.23848			(+)	(+)	RCCC
N-acetylneuramite pyruvate lyase	1.325459			(+)		
NCK-associated protein 1		0.004	1.4471	(+)		
nestin --pendin	1.226027			(+)		
neural precursor cell expressed, developmentally down-regulated gene 4a		0.004	0.7168	(-)		
neural proliferation, differentiation and control gene 1	1.34827	0.037	1.263	(+)	(+)	RCCC
neuro guanine nucleotide exchange factor	0.773454			(-)		
neuropilin		0.031	1.3972	(+)	(+)	RCCC
neutrophil cytosolic factor 2	1.233541			(+)		
Ngfi-A binding protein 2		0.049	1.2723	(+)		
nicotinamide nucleotide transhydrogense	0.542394	8E-04	0.5672	(-)	(-)	RCCC
nidogen 1		0.003	1.5346	(+)	(+)	RCCC
NIMA (never in mitosis gene a)-related expressed kase 6	1.464337			(+)		
N-myc downstream regulated 2	0.598324	0.003	0.7062	(-)		
non-catalytic region of tyrosine kase adaptor protein 1		0.005	1.3379	(+)	(+)	RCCC
nuclear factor of kappa light chain gene enhancer in B-cells 1, p105		0.009	1.4106	(+)		
nuclear protein 15.6	0.771762			(-)		
nuclear receptor coactivator 4		0.034	0.6812	(-)	(+)	RCCDC
nuclear receptor subfamily 2, group F, member 2		0.011	1.3455	(+)	(+)	RCCC
nuclear receptor subfamily 2, group F, member 6		0.036	1.2859	(+)	(-)	RCCDC

nuclease sensitive element binding protein 1	1.47757			(+)	(+)	RCCC
nucleophosmin 1	1.441561	8E-04	1.6685	(+)	(+)	RCCC
numb gene homolog (Drosophila)	1.591483			(+)		
oncostatin receptor	1.348268	8E-04	2.0715	(+)		
opioid growth factor receptor	1.198578			(+)		
ornithine aminotransferase		0.022	0.7587	(-)		
ornithine decarboxylase, structural	1.312592			(+)		
osteomodulin	0.828403			(-)		
oxysterol binding protein-like 1A	0.670761	0.01	0.6983	(-)		
pantophysin	0.644709	9E-04	0.6323	(-)		
papillary rel cell carcinoma (translocation-associated)		0.002	1.4613	(+)	(?)	RCC conflict
parvalbumin	0.507541			(-)	(+)/(-)	RCC conflict
PC4 and SFRS1 interacting protein 2 (expressed sequence AU015605)	1.201167			(+)		
PCTAIRE-motif protein kise 3	0.808356			(-)	(+)	RCC DC
peptidylprolyl isomerase (cyclophilin)-like 1	1.194882			(+)	(+)	RCCC
peptidylprolyl isomerase C	0.855714			(-)		
peptidylprolyl isomerase C-associated protein		0.004	1.6664	(+)	(+)	RCCC
period homolog 1 (Drosophila)		0.0008	0.5522979	(-)		
		0.0305	0.7390266			
period homolog 2 (Drosophila)		0.005	0.6496	(-)		
peroxiredoxin 5	1.36499			(+)	(?)	RCC conflict
peroxisomal biogenesis factor 13	0.827587			(-)		
peroxisomal delta3, delta2-enoyl-Coenzyme A isomerase	0.732094			(-)	(-)	RCCC
peroxisomal membrane protein 2, 22 kDa	0.671027			(-)	(+)/(-)	RCC conflict
peroxisomal sarcosine oxidase	0.675459			(-)	(-)	RCCC
peroxisome proliferator activated receptor alpha	0.605623			(-)		
PH domain containing protein in reti 1	0.770569			(-)		
phenylalanine hydroxylase	0.483001	8E-04	0.4244	(-)	(-)	RCCC
phenylalkylamine Ca2+ antagonist (emopamil) binding protein	0.701194			(-)		
phorbol-12-myristate-13-acetate-induced protein 1	1.320285	0.047	1.3734	(+)		
phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 1 (p85 alpha)	1.234427			(+)		
phosphatidylinositol transfer protein	1.356671			(+)		
phosphodiesterase 1A, calmodulin-dependent	0.832816			(-)	(-)	RCCC
phosphofructokinase, liver, B-type	0.836516			(-)		
phosphoglycerate kise 1	0.83983			(-)	(+)	RCC DC
phosphoglycerate mutase 2	0.435688	0.044	0.6904	(-)		
phospholipase A2, activating protein	1.249295			(+)		

phospholipase A2, group IB, pancreas	1.706747		(+)			
phospholipase A2, group IIA (platelets, synovial fluid)	0.841435		(-)			
phospholipid scramblase 1	1.634313		(+)	(+)	RCC	C
phosphoprotein enriched in astrocytes 15	2.04807		(+)	(+)	RCC	C
phytanoyl-CoA hydroxylase	0.706937		(-)	(-)	RCC	C
plasminogen activator, tissue		0.02	1.423(+)	(-)	RCC	DC
platelet derived growth factor receptor, beta polypeptide	1.386991		(+)			
platelet derived growth factor, alpha		0.014	1.327(+)			
platelet derived growth factor, B polypeptide		8E-04	1.6569(+)	(+)	RCC	C
platelet factor 4	1.959063	0.036	1.5766(+)			
platelet-activating factor acetylhydrolase, isoform 1b, alpha1 subunit		8E-04	1.462(+)			
poliovirus receptor-related 3	1.277304; 1.163199		(+)	(+)	RCC	C
poly (A) polymerase alpha	0.455758	0.009	0.6839(-)	(+)	RCC	DC
poly(rC) binding protein 1	1.229561		(+)	(+)	RCCC	
polycystic kidney disease 1 homolog	0.861306		(-)	(+)	RCC	DC
polymerase, gamma		0.041	0.758(-)			
polypyrimidine tract binding protein 1	1.187485		(+)	(+)	RCCC	
potassium channel, subfamily K, member 2	0.816677		(-)			
PPAR gamma coactivator-1beta protein	0.752031		(-)			
prion protein		0.015	0.6883(-)			
procollagen lysine, 2-oxoglutarate 5- dioxygenase 2	1.236481		(+)	(+)	RCCC	
procollagen, type I, alpha 1		8E-04	4.1081(+)	(+)(-?)	RCC	conflict
procollagen, type I, alpha 2		8E-04	2.8442(+)	(+)	RCCC	
procollagen, type IV, alpha 1	1.962618	0.003	2.2032(+)	(+)	RCCC	
procollagen, type IV, alpha 2		0.032	1.8088(+)	(+)	RCCC	
procollagen, type V, alpha 1	1.363199		(+)	(+)	RCCC	
procollagen, type V, alpha 2	1.555847	8E-04	1.4432(+)	(+)	RCCC	
prohibitin	0.875224		(-)			
proline dehydrogenase	0.555697	8E-04	0.5546(-)			
protease (prosome, macropain) 26S subunit, ATPase 1	1.274107		(+)			
proteasome (prosome, macropain) 28 subunit, 3	0.545487		(-)			
proteasome (prosome, macropain) 26S subunit, non-ATPase, 10	1.249655		(+)			
proteasome (prosome, macropain) 26S subunit, non-ATPase, 13	1.274187		(+)	(+)	RCCC	
proteasome (prosome, macropain) 28 subunit, alpha	1.412928	9E-04	1.7167(+)			
proteasome (prosome, macropain) subunit, alpha type 2	1.318854		(+)			
proteasome (prosome, macropain) subunit, alpha type 6	1.252206		(+)	(+)	RCCC	
proteasome (prosome, macropain)		0.013	1.3768(+)	(+)	RCCC	



subunit, alpha type 7						
proteasome (prosome, macropain)		0.015	1.3622	(+)		
subunit, beta type 1						
proteasome (prosome, macropain)		0.003	1.5053	(+)	(+)	RCCC
subunit, beta type 10						
protein C	0.716043			(-)	(-)	RCCC
protein kise C, delta		0.009	1.3244	(+)	(+)	RCCC
protein phosphatase 1, catalytic						
subunit, alpha isoform	1.477029			(+)		
protein phosphatase 1, regulatory						
(inhibitor) subunit 1A	0.393414			(-)		
protein phosphatase 2a, catalytic						
subunit, beta isoform	1.289147			(+)	(-)	RCCDC
protein phosphatase 3, catalytic						
subunit, gamma isoform	0.858408			(-)		
protein S (alpha)		8E-04	1.7106	(+)		
protein tyrosine phosphatase 4a1						
subunit, alpha isoform	1.499428			(+)		
protein tyrosine phosphatase, non-						
receptor type 9	1.212579	0.038	1.2656	(+)		
protein tyrosine phosphatase, receptor						
type, B	0.830019			(-)	(+)	RCCDC
protein tyrosine phosphatase, receptor						
type, C	1.214849	0.002	1.5928	(+)		
protein tyrosine phosphatase, receptor						
type, C polypeptide-associated		0.001	1.6535	(+)		
protein						
protein tyrosine phosphatase, receptor		0.007	1.2743	(+)	(-)	RCCDC
type, O						
proteoglycan, secretory granule						
subunit, alpha isoform	1.368298			(+)	(+)	RCCC
proteasome (prosome, macropain)		0.005	1.8412	(+)	(+)	RCCC
subunit, beta type 8 (large						
multifunctional protease 7)						
prothymosin alpha	1.383187	8E-04	1.5311	(+)	(+)	RCCC
purinergic receptor (family A group						
5); RIKEN cD 2610302102 gene		0.029	1.2282	(+)		
pyridoxal (pyridoxine, vitamin B6)						
kise	1.569586			(+)		
PYRIN-containing APAF1-like						
protein 5 / expressed sequence		0.005	0.6865	(-)		
A1504961						
pyruvate decarboxylase		0.026	0.6537	(-)		
pyruvate dehydrogenase 2						
subunit, alpha isoform	0.566341			(-)		
pyruvate kise 3		1.368806		(+)		
pyruvate kise liver and red blood cell						
R binding motif protein 3	0.83514	0.004	0.7669	(-)	(-)	RCCC
R polymerase I associated factor, 53						
kD	2.299533	8E-04	1.6893	(+)		
R polymerase II 1						
subunit, alpha isoform	1.348222			(+)		
RAB11a, member RAS oncogene						
family	0.808996			(-)		
RAB3D, member RAS oncogene						
family	1.160313			(+)	(+)	RCCC
Ral-interacting protein 1		0.013	1.212	(+)		
	1.278257			(+)	(-)	RCCDC



ribosomal protein L8	1.476231		(+)	(+)	RCCC
ribosomal protein S14		0.004	1.7229	(+)	RCCC
ribosomal protein S15	1.867474	8E-04	1.6115	(+)	
ribosomal protein S15	1.566886		(+)		
ribosomal protein S16	1.95787	0.001	1.572	(+)	RCCC
ribosomal protein S19	1.616338		(+)	(+)	RCCC
ribosomal protein S2	1.8787		(+)	(+)	RCCC
ribosomal protein S23	1.379952	8E-04	1.4732	(+)	RCCC
ribosomal protein S26	1.468534		(+)		
ribosomal protein S29		0.027	1.4417	(+)	
ribosomal protein S3	1.528904		(+)	(+)	RCCC
ribosomal protein S3a	1.878501	8E-04	1.4223	(+)	RCCC
ribosomal protein S4, X-linked	1.873272	8E-04	1.607	(+)	
ribosomal protein S5		8E-04	1.9502	(+)	
ribosomal protein S6	1.637744; 1.663683	0.0008; 0.0251	1.416617; 1.63716	(+)	
ribosomal protein S6 kise, 90kD, polypeptide 4	1.345873		(+)		
ribosomal protein S7	1.886875	0.002	1.6322	(+)	
ribosomal protein, large P2		0.004	1.4626	(+)	RCCC
ribosomal protein, large, P1	2.003644	0.029	1.7745	(+)	RCCC
RIKEN cD 0610006F02 gene		0.0008; 0.0489	0.6493102; 0.7666818	(-)	
RIKEN cD 0610006N12 gene	0.783579		(-)		
RIKEN cD 0610007L01 gene	1.194059		(+)		
RIKEN cD 0610011C19 gene	0.753755		(-)		
RIKEN cD 0610016J10 gene	1.384281		(+)		
RIKEN cD 0610025G13 gene	1.618142	0.004	1.4677	(+)	RCC conflict
RIKEN cD 0610025I19 gene	0.573976	0.044	0.7207	(-)	
RIKEN cD 0610041E09 gene	1.318886		(+)		
RIKEN cD 1010001M04 gene	0.701714		(-)		
RIKEN cD 1100001F19 gene	1.367751		(+)		
RIKEN cD 1100001J13 gene - pending	0.821539		(-)	(+)	RCC DC
RIKEN cD 1110001I24 gene	1.385664	0.029	1.2197	(+)	
RIKEN cD 1110002C08 gene	0.801259		(-)		
RIKEN cD 1110005N04 gene		0.012	1.2392	(+)	
RIKEN cD 1110007F23 gene		0.007	1.2275	(+)	
RIKEN cD 1110008B24 gene		0.002	1.3502	(+)	
RIKEN cD 1110014C03 gene	1.449833		(+)		
RIKEN cD 1110020L19 gene	1.199686		(+)		
RIKEN cD 1110032A13 gene		8E-04	1.9945	(+)	
RIKEN cD 1110038J12 gene	0.786088	0.01	0.7623	(-)	
RIKEN cD 1110038L14 gene	1.460735		(+)	(+)	RCCC
RIKEN cD 1110054A24 gene	1.386487		(+)		
RIKEN cD 1190006C12 gene		0.002	1.5092	(+)	
RIKEN cD 1200003E16 gene	0.827166		(-)		
RIKEN cD 1200009B18 gene		0.013	1.3411	(+)	
RIKEN cD 1200011D11 gene	0.569291		(-)		
RIKEN cD 1200013A08 gene		8E-04	1.549	(+)	
RIKEN cD 1200014D15 gene	0.489823	0.031	0.6793	(-)	

RIKEN cD 1200014I03 gene	1.383879			(+)		
RIKEN cD 1200015A22 gene	1.226764			(+)		
RIKEN cD 1200016G03 gene	0.828808			(-)		
RIKEN cD 1300002P22 gene	0.510225			(-)		
RIKEN cD 1300004O04 gene	0.761224	0.005	0.7406	(-)		
RIKEN cD 1300013F15 gene		0.021	0.684	(-)		
RIKEN cD 1300013G12 gene	1.228874			(+)		
RIKEN cD 1300017C12 gene	0.785174			(-)	(-)	RCC C
RIKEN cD 1300018I05 gene	1.252751			(+)		
RIKEN cD 1300019I21 gene	1.245337			(+)		
RIKEN cD 1500010B24 gene		0.002; 0.002	1.398499; 1.411263	(+)	(+)	RCC C
RIKEN cD 1500026A19 gene	1.180374			(+)		
RIKEN cD 1500041J02 gene	0.781326	0.04	0.7179	(-)		
RIKEN cD 1700008H23 gene		0.029	0.8204	(-)		
RIKEN cD 1700012B18 gene	0.660943			(-)		
RIKEN cD 1700015P13 gene		0.04	0.7114	(-)		
RIKEN cD 1700016A15 gene		0.026	1.2838	(+)		
RIKEN cD 1700028A24 gene	0.705073			(-)		
RIKEN cD 1700037H04 gene	1.138844			(+)		
RIKEN cD 1810009M01 gene	2.104826			(+)		
RIKEN cD 1810013B01 gene	0.61166			(-)		
RIKEN cD 1810023B24 gene	1.264664			(+)		
RIKEN cD 1810027P18 gene	0.601175			(-)	(-)	RCC C
RIKEN cD 1810036E22 gene	0.70486			(-)		
RIKEN cD 1810038D15 gene	1.282694			(+)		
RIKEN cD 1810043O07 gene		0.004	1.2972	(+)		
RIKEN cD 1810054O13 gene	0.67673			(-)		
RIKEN cD 1810058K22 gene	1.378858			(+)		
RIKEN cD 2010012D11 gene	0.716885	0.003	0.6902	(-)		
RIKEN cD 2010315L10 gene	1.204993			(+)		
RIKEN cD 2310001A20 gene	0.726674			(-)		
RIKEN cD 2310004I03 gene	0.812809			(-)		
RIKEN cD 2310004L02 gene	0.767893	0.009	0.7563	(-)		
RIKEN cD 2310009E04 gene	0.619409	0.03	0.7724	(-)		
RIKEN cD 2310010G13 gene	0.90919			(-)		
RIKEN cD 2310022K15 gene		0.042	1.2791	(+)		
RIKEN cD 2310032J20 gene	0.456694			(-)		
RIKEN cD 2310046G15 gene		0.013	1.3684	(+)	(+)	RCC C
RIKEN cD 2310051E17 gene	0.616314			(-)		
RIKEN cD 2310067B10 gene	0.805886			(-)		
RIKEN cD 2310075M15 gene	1.253001	0.0290	1.3141	(+)		
RIKEN cD 2310079C17 gene	1.178546			(+)		
RIKEN cD 2410002J21 gene	1.358002			(+)		
RIKEN cD 2410021P16 gene	0.679461			(-)		
RIKEN cD 2410026K10 gene		8E-04	1.9506	(+)		
RIKEN cD 2410029D23 gene	0.774382			(-)		
RIKEN cD 2410129E14 gene		8E-04	2.0517	(+)		
RIKEN cD 2410174K12 gene		0.036	1.3316	(+)		
RIKEN cD 2510015F01 gene	1.566621			(+)		
RIKEN cD 2600001N01 gene	1.259811			(+)		

RIKEN cD 2600015J22 gene		0.004	1.6201	(+)			
RIKEN cD 2600017H24 gene	1.480539			(+)			
RIKEN cD 2610007A16 gene	0.706068			(-)			
RIKEN cD 2610029K21 gene	1.159174			(+)			
RIKEN cD 2610039E05 gene	0.776991			(-)			
RIKEN cD 2610200M23 gene		0.003	1.4284	(+)	(+)	RCCC	
RIKEN cD 2610206D03 gene	1.27124			(+)			
RIKEN cD 2610301D06 gene	1.849151			(+)			
RIKEN cD 2610305D13 gene	2.013008			(+)			
RIKEN cD 2610306D21 gene		0.038	1.3795	(+)			
RIKEN cD 2610511O17 gene	1.177157			(+)			
RIKEN cD 2610524G07 gene	0.702826			(-)			
RIKEN cD 2610524G09 gene	1.175638			(+)			
RIKEN cD 2700027J02 gene	1.235225			(+)			
RIKEN cD 2700038K18 gene		0.003	1.5276	(+)			
RIKEN cD 2700038M07 gene - pending		8E-04	1.9098	(+)	(-)	RCCDC	
RIKEN cD 2700055K07 gene		0.029	1.3762	(+)			
RIKEN cD 2700099C19 gene	1.141995			(+)			
RIKEN cD 2810004N23 gene	1.296022			(+)			
RIKEN cD 2810047L02 gene	1.371268			(+)			
RIKEN cD 2810409H07 gene	1.352519			(+)			
RIKEN cD 2810411G23 gene	1.327569			(+)	(+)	RCCC	
RIKEN cD 2810418N01 gene		0.004	1.4296	(+)			
RIKEN cD 2810430J06 gene		0.038	1.3085	(+)			
RIKEN cD 2810468K17 gene		0.022	1.185	(+)			
RIKEN cD 2810473M14 gene	0.624595			(-)			
RIKEN cD 2900074L19 gene		0.049	0.706	(-)			
RIKEN cD 3010001A07 gene	0.829789			(-)			
RIKEN cD 3010027G13 gene	0.765137			(-)			
RIKEN cD 3021401A05 gene	1.605988	8E-04	3.0674	(+)			
RIKEN cD 3110001N18 gene		9E-04	1.3959	(+)	(+)	RCCC	
RIKEN cD 3230402E02 gene	1.291597			(+)	(+)	RCCC	
RIKEN cD 3321401G04 gene		0.029	1.3004	(+)			
RIKEN cD 4430402G14 gene	1.473069	8E-04	1.4996	(+)			
RIKEN cD 4632401C08 gene	0.547074			(-)			
RIKEN cD 4733401N12 gene		0.03	1.2321	(+)			
RIKEN cD 4921528E07 gene		0.039	1.2027	(+)			
RIKEN cD 4921537D05 gene	1.258399			(+)			
RIKEN cD 4930506M07 gene	1.233212			(+)			
RIKEN cD 4930533K18 gene	1.325535	0.004	1.4196	(+)			
RIKEN cD 4930542G03 gene	1.660924			(+)			
RIKEN cD 4930552N12 gene	0.625191	0.01	0.7235	(-)			
RIKEN cD 4930579A11 gene	1.743458			(+)	(+)	RCCC	
RIKEN cD 4932442K08 gene		0.05	1.1747	(+)			
RIKEN cD 4933405K01 gene	1.215798			(+)			
RIKEN cD 5031412I06 gene	1.528882			(+)			
RIKEN cD 5031422I09 gene	0.71728	0.036	0.755	(-)			
RIKEN cD 5133400A03 gene	1.242284	0.005	1.6697	(+)			
RIKEN cD 5133401H06 gene	0.796236			(-)			
RIKEN cD 5430416A05 gene	1.253096			(+)			

RIKEN cD 5630401J11 gene		0.002	1.4714(+)			
RIKEN cD 5730403B10 gene	0.817117		(-)	(+)	RCC	DC
RIKEN cD 5730406G15 gene		0.006	1.3059(+)			
RIKEN cD 5730534O06 gene	0.777482		(-)			
RIKEN cD 5830445O15 gene	0.839158		(-)			
RIKEN cD 6230410T01 gene		0.008	1.354(+)			
RIKEN cD 6330565B14 gene	0.484948	0.002	0.5883(-)			
RIKEN cD 6330583M11 gene	3.025888	8E-04	2.0304(+)	(+)	RCC	C
RIKEN cD 6430559E15 gene	0.797784		(-)			
RIKEN cD 6530411B15 gene	0.748059	8E-04	0.6185(-)			
RIKEN cD 6720463E02 gene	1.241163		(+)			
RIKEN cD 9130011J04 gene		0.002	1.4288(+)			
RIKEN cD 9130022E05 gene	0.798272		(-)			
RIKEN cD 9530058B02 gene	0.6242	0.05	0.7595(-)			
RIKEN cD 9530089B04 gene	0.680734	8E-04	0.5543(-)			
RIKEN cD A230106A15 gene	0.855558		(-)			
RIKEN cD A330103N21 gene	0.7567217; 0.700483		(-)			
RIKEN cD A930008K15 gene	0.712949		(-)			
RIKEN cD D630002J15 gene	0.776514		(-)			
RIKEN cD E130113K08 gene		0.046	1.3068(+)			
ring finger protein (C3HC4 type) 19		0.003	1.3119(+)			
runx related transcription factor 1		0.012	1.3557(+)			
S100 calcium binding protein A10 (calpactin)	3.102836	0.002	1.7328(+)			
S100 calcium binding protein A13		0.033	1.2577(+)			
S100 calcium binding protein A4	1.715886	0.023	1.4938(+)			
S100 calcium binding protein A6 (calcylin)	7.344924	8E-04	3.3762(+)			
S-adenosylhomocysteine hydrolase		0.004	0.6135(-)	(-)	RCC	C
SAR1a gene homolog (S. cerevisiae)	1.167781		(+)	(-)	RCC	DC
schlafen 4	1.159855		(+)			
SEC13 related gene (S. cerevisiae)	1.144426		(+)			
RIKEN cD 1110003H02 gene						
SEC61, gamma subunit (S. cerevisiae)	1.389586		(+)	(+)(-)	RCC	conflict
secreted acidic cysteine rich glycoprotein	2.276906	0.002	2.352(+)	(+)	RCC	C
secreted and transmembrane 1		0.033	0.7896(-)			
secreted phosphoprotein 1	5.051855		(+)	(-)(+)	RCC	conflict
selectin, platelet (p-selectin) ligand		0.029	1.3367(+)	(+)	RCC	C
selenium binding protein 2		0.003	0.5856(-)	(-)	RCC	C
selenophosphate synthetase 2		0.014	0.7176(-)	(-)	RCC	C
selenoprotein P, plasma, 1	0.591423		(-)	(-)	RCC	C
sepin 8	1.222963		(+)			
serine (or cysteine) protease inhibitor, clade B (ovalbumin), member 2	1.143231		(+)			
serine (or cysteine) protease inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2		8E-04	1.808(+)			
serine (or cysteine) protease inhibitor, clade G (C1 inhibitor), member 1		9E-04	2.3765(+)	(+)	RCC	C

serine (or cysteine) protease inhibitor, clade H (heat shock protein 47), member 1	2.222691	8E-04	1.7609(+)			
serine hydroxymethyl transferase 1 (soluble)		0.013	0.7234(-)	(+)	RCC	DC
serine hydroxymethyl transferase 2 (mitochondrial); RIKEN cD 2700043D08 gene	0.700444	0.035	0.6911(-)	(+)	RCC	DC
serine palmitoyltransferase, long chain base subunit 1	0.869628		(-)	(+)	RCC	DC
serine protease inhibitor 6		0.049	1.5971(+)			
serine protease inhibitor, Kunitz type 1	1.199628		(+)			
serine protease inhibitor, Kunitz type 2	1.224878		(+)			
serine/arginine repetitive matrix 1	1.214449		(+)			
serine/threonine kinase receptor associated protein	1.229013		(+)			
serine/threonine protein kinase CISK	1.188914		(+)			
serum amyloid A 3	2.072529		(+)			
serum/glucocorticoid regulated kinase		8E-04	0.4203(-)			
serum/glucocorticoid regulated kinase 2	0.560278	0.01	0.601(-)			
SET translocation	1.219476		(+)	(+)	RCC	C
sex-lethal interactor homolog (Drosophila)	0.598624	8E-04	0.4427(-)			
SFFV proviral integration 1		0.006	1.6359(+)			
SH3 domain binding glutamic acid-rich protein-like 3	2.196369	8E-04	2.0402(+)			
SH3 domain protein 3	1.2681		(+)			
sideroflexin 1	0.866365		(-)			
sigl sequence receptor, delta	1.316856	0.014	1.4178(+)	(+)	RCC	C
sigl transducer and activator of transcription 3		0.01	1.3489(+)	(+)	RCC	C
sigling intermediate in Toll pathway-evolutionarily conserved		0.002	0.7132(-)	(-)	RCC	C
single Ig IL-1 receptor related protein		0.037	0.8027(-)	(-)	RCC	C
slit homolog 2 (Drosophila)	0.70698		(-)			
slit homolog 3 (Drosophila)		0.017	1.3421(+)			
small inducible cytokine A2	2.206498	8E-04	2.3421(+)			
small inducible cytokine A5		0.003	1.7713(+)	(+)	RCC	C
small inducible cytokine A7		0.019	1.4822(+)			
small inducible cytokine A9	1.750569	0.002	1.5855(+)			
small inducible cytokine B subfamily (Cys-X-Cys), member 10	2.175863	8E-04	2.2946(+)			
small inducible cytokine B subfamily, member 5		0.022	1.3809(+)			
small inducible cytokine subfamily D, 1	1.38781	0.002	1.5826(+)			
small nuclear ribonucleoprotein D2	1.387716	0.006	1.4984(+)	(+)	RCC	C
small nuclear ribonucleoprotein E		8E-04	1.4505(+)	(+)	RCC	C
small nuclear ribonucleoprotein polypeptide G	1.418612	8E-04	1.3907(+)			
small proline-rich protein 1A		8E-04	2.4047(+)			
SMC (structural maintenance of chromosomes 1)-like 1 (S. cerevisiae)	1.219049		(+)	(-)	RCC	DC

smoothelin	1.369266		(+)			
smoothed homolog (Drosophila)		0.036	0.6399(-)			
soc-2 (suppressor of clear) homolog (C. elegans)		0.04	1.2812(+)			
solute carrier family 1, member 1		0.006	1.2973(+)	(-)	RCC	DC
solute carrier family 12, member 1	0.278552		(-)	(-)	RCC	C
solute carrier family 13 (sodium/sulphate symporters), member 1	1.820774	0.001	1.5263(+)			
solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3	0.6572	0.041	0.6979(-)	(-)	RCCC	
solute carrier family 15 (H <sup>+</sup> /peptide transporter), member 2	0.639301		(-)			
solute carrier family 16 (monocarboxylic acid transporters), member 2	0.715352		(-)	(-)	RCCC	
solute carrier family 16 (monocarboxylic acid transporters), member 7		0.009	0.6846(-)	(+)	RCC	DC
solute carrier family 2 (facilitated glucose transporter), member 5		0.047	0.6263(-)	(-)	RCCC	
solute carrier family 22 (organic anion transporter), member 6		0.013	0.6199(-)	(-)	RCCC	
solute carrier family 22 (organic anion transporter), member 8 / (Roc) reduced in osteosclerosis transporter	0.404831	0.014	0.5437(-)	(-)	RCCC	
solute carrier family 22 (organic cation transporter), member 1	0.645465	9E-04	0.6281(-)	(+)	RCC	DC
solute carrier family 22 (organic cation transporter), member 1-like	0.486263	0.001	0.6191(-)	(-)(+)	RCC	conflict
solute carrier family 22 (organic cation transporter), member 2	0.630304	0.004	0.6553(-)			
solute carrier family 22 (organic cation transporter), member 4		0.003	0.6747(-)			
solute carrier family 22 (organic cation transporter), member 5	0.513612	0.002	0.5857(-)			
solute carrier family 22 (organic cation transporter)-like 2	0.663072		(-)			
solute carrier family 25 (mitochondrial carrier	0.616166		(-)			
solute carrier family 25 (mitochondrial carrier		0.006	0.7117(-)			
solute carrier family 25 (mitochondrial deoxynucleotide carrier), member 19	0.753628		(-)			
solute carrier family 26, member 4	0.713201	8E-04	0.6303(-)			
solute carrier family 27 (fatty acid transporter), member 2	0.586465	0.013	0.5879(-)			
solute carrier family 3, member 1		0.029	0.6994(-)	(-)	RCCC	
solute carrier family 31, member 1	0.850953		(-)			
solute carrier family 34 (sodium phosphate), member 1	0.536109		(-)			
solute carrier family 34 (sodium phosphate), member 2		8E-04	1.678(+)			
solute carrier family 35, member A5; RIKEN cD 1010001J06 gene	0.860405		(-)			



solute carrier family 4 (anion exchanger), member 4	0.642787	0.01	0.6624(-)	(-)	RCCC
solute carrier family 6 (neurotransmitter transporter, glycine), member 9 / glycine transporter 1	1.136822		(+)		
solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 7	0.832285	0.046	0.7065(-)	(-)	RCCC
solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 9	0.668683	8E-04	0.6346(-)		
speckle-type POZ protein	0.811261		(-)		
spermatogenesis associated factor	1.246927		(+)		
spermidine synthase	1.524323		(+)		
spermidine/spermine N1-acetyl transferase		0.036	1.3351(+)		
sphingomyelin phosphodiesterase 2, neutral	0.730054		(-)		
splicing factor 3b, subunit 1, 155 kDa	1.256915	0.028	1.386(+)	(+)	RCCC
splicing factor, arginine/serine-rich 2 (SC-35)	1.228873		(+)	(+)	RCCC
split hand/foot deleted gene 1		0.002	1.2817(+)	(+)	RCCC
src homology 2 domain-containing transforming protein D	0.826156		(-)		
src-like adaptor protein	1.212423		(+)		
stearoyl-Coenzyme A desaturase 1	0.26606	8E-04	0.4177(-)		
steroid receptor R activator 1	1.155368		(+)		
sterol carrier protein 2, liver	0.659454	0.039	0.6361(-)	(+)	RCCDC
striatin, calmodulin binding protein 4 / expressed sequence C80611		0.015	1.3823(+)		
stromal cell derived factor 1	0.638758		(-)		
succinate dehydrogenase complex, subunit B, iron sulfur (Ip); RIKEN cD 0710008N11 gene	0.650889		(-)	(-)	RCCC
succinate dehydrogenase complex, subunit A, flavoprotein (Fp)	0.63565		(-)		
succinate-Coenzyme A ligase, ADP-forming, beta subunit	0.738104		(-)		
succinate-Coenzyme A ligase, GDP-forming, beta subunit	0.8423		(-)		
sulfotransferase-related protein SULT-X1		0.017	1.2358(+)		
superoxide dismutase 2, mitochondrial	0.627202	0.023	0.6795(-)	(+)	RCCDC
surfeit gene 4	1.173262		(+)	(+)	RCCC
SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5	1.34736; 1.192875		(+)	(+)	RCCC
SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 1	1.375898		(+)	(+)	RCCC
syndecan 1	1.755052		(+)	(-)	RCCDC
syntrophin, basic 2	1.145842		(+)		
TAF10 R polymerase II, TATA box binding protein (TBP)-associated	1.437509		(+)		

factor, 30 kDa						
TAF9 R polymerase II, TATA box binding protein (TBP)-associated factor, 32 kDa	1.315523			(+)		
tal1 2	0.590195	8E-04	0.5429(-)			
TATA box binding protein-like protein		0.007	1.336(+)			
T-box 6	1.613638	8E-04	1.8123(+)			
T-cell specific GTPase		0.003	2.029(+)			
T-cell, immune regulator 1		9E-04	1.3678(+)			
TEA domain family member 2	1.218905			(+)		
tescin C	2.161393	8E-04	2.1224(+)			
tescin XB	0.81373			(-)		
testis derived transcript	1.466866			(+)	(+)	RCCC
tetranectin (plasminogen binding protein)	0.69379			(-)		
tetratricopeptide repeat domain		0.032	1.3798(+)		(+)	RCCC
TG interacting factor	1.49248	8E-04	1.6651(+)		(+)	RCCC
thiamin pyrophosphokinase	0.815518			(-)		
thioesterase, adipose associated	0.608099	8E-04	0.4926(-)			
thioether S-methyltransferase		0.002	0.4638(-)			
thioredoxin 1	1.547693	0.025	1.52(+)		(-)/(+)	RCC conflict
thioredoxin 2		0.006	0.7742(-)			
thioredoxin-like (32kD)	1.285715			(+)		
thrombospondin 1		0.003	1.7297(+)		(-)	RCCDC
thymidine kinase 1	1.822689			(+)	(+)	RCCC
thymoma viral proto-oncogene 1	1.502028			(+)	(+)	RCCC
thymosin, beta 4, X chromosome	2.365009	8E-04	2.6847(+)		(+)	C
thyroid hormone responsive SPOT14 homolog (Rattus)	0.293263	8E-04	0.4343(-)			
Ti11 cytotoxic granule-associated R binding protein-like 1	1.21967			(+)	(+)	RCCC
tight junction protein 2		0.015	1.4429(+)		(-)	RCCDC
tissue inhibitor of metalloprotease	2.944279	8E-04	2.854(+)		(+)	RCCC
Tnf receptor-associated factor 2	1.31305			(+)		
toll-like receptor 2		0.014	1.4711(+)			
topoisomerase (D) III beta	0.840401			(-)		
TRAF-interacting protein	1.192268			(+)		
transcobalamin 2	0.522163	8E-04	0.5031(-)		(-)	RCCC
transcription elongation factor A (SII), 3	0.789024			(-)		
transcription elongation regulator 1 (CA150)	5.521204	8E-04	3.3877(+)			
transcription factor 21		8E-04	1.7517(+)		(-)	RCCDC
transcription factor 4		0.016	1.3902(+)			
transcription factor Dp 1		0.003	1.3295(+)		(+)	RCCC
transformation related protein 53	1.362828			(+)	(+)/(--?)	RCC conflict
transformed mouse 3T3 cell double minute 2		0.044	1.3109(+)		(+)	RCCC
transforming growth factor beta 1 induced transcript 4	2.395573	0.008	1.5674(+)		(+)	RCCC

transforming growth factor, beta induced, 68 kDa	2.085258	8E-04	1.8572	(+)	(+)	RCCC
transgelin	1.600162	8E-04	2.5038	(+)		
translin	1.191429			(+)		
transmembrane 7 superfamily member 1	0.786219			(-)		
transmembrane protein 8 (five membrane-spanning domains)	0.7753253; 0.7539193	0.023	0.6612	(-)		
Trans-prenyltransferase		0.003	1.3624	(+)		
transthyretin	0.592428			(-)		
trinucleotide repeat containing 11 (IHR-associated protein, 230 kDa subunit)		0.028	1.3829	(+)		
tropomyosin 2, beta	1.834774			(+)		
tropomyosin 3, gamma	2.00637	8E-04	1.5813	(+)		
tubulin alpha 1		8E-04	2.2002	(+)		
tubulin alpha 2	2.656871	0.002	2.0093	(+)		
tubulin, beta 5	3.080405			(+)	(+)	RCCC
tuftelin 1	1.497479			(+)		
tumor necrosis factor receptor superfamily, member 10b	1.355122			(+)		
tumor necrosis factor receptor superfamily, member 1a	1.431735	0.021	1.3333	(+)	(+)	RCCC
tumor necrosis factor receptor superfamily, member 1b		0.024	1.3824	(+)		
tumor protein p53 binding protein, 2 / expressed sequence A1746547		0.01	0.6437	(-)		
tumor rejection antigen gp96	1.322746			(+)	(+)	RCCC
tumor-associated calcium sigl transducer 2	2.166496	0.002	1.6128	(+)	(-)	RCCDC
tural killer tumor recognition sequence	1.678022	8E-04	2.0726	(+)		
TYRO protein tyrosine kinase binding protein	1.850489	8E-04	2.1288	(+)	(+)	RCCC
tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide	1.374164			(+)		
tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide	1.598302	0.005	1.5449	(+)	(+)	RCCC
ubiquitin specific protease 2	0.387442	8E-04	0.4121	(-)	(-)	RCCC
ubiquitin specific protease 7 (expressed sequence AA409944)	1.368404			(+)		
ubiquitin-conjugating enzyme E2D 2		0.009	1.3738	(+)		
ubiquitin-conjugating enzyme E2H	1.73032	0.002	1.6531	(+)	(+)	RCCC
ubiquitin-conjugating enzyme E2I	1.501533			(+)		
ubiquitin-conjugating enzyme E2L 3	1.276359			(+)		
ubiquitin-conjugating enzyme E2N	1.253604	0.008	1.3224	(+)		
ubiquitin-like 1	1.235698			(+)	(+)	RCCC
ubiquitin-like 1 (sentrin) activating enzyme E1A	1.209625			(+)	(+)	RCCC
ubiquitin-like 1 (sentrin) activating enzyme E1B	1.319403			(+)		
UDP-Gal:beta-Gluc beta 1,3-galactosyltransferase, polypeptide 3	0.790361			(-)		

UDP-Gal:betaGlc beta 1,4-galactosyltransferase, polypeptide 2	1.226956			(+)			
UDP-N-acetyl-alpha-D-galactosamine:(N-acetylneuraminy)-galactosylglucosylceramide-beta-1, 4-N-acetylgalactosaminyltransferase	1.374851	0.031	1.4925	(+)			
Unknown	1.631964	8E-04	1.8313	(+)			
Unknown	1.452741	0.012	1.5847	(+)			
Unknown	1.622317	0.001	1.369	(+)			
Unknown	0.196028	0.019	0.4352	(-)			
Unknown	1.599236; 1.758187	0.0008; 0.0008	1.871876; 2.313198	(+)			
Unknown	1.288468	8E-04	1.4377	(+)			
Unknown	0.665629	0.013	0.6782	(-)			
Unknown	1.361226	0.003	1.4285	(+)			
Unknown	1.196485	9E-04	1.556	(+)			
Unknown	1.555723	8E-04	1.9514	(+)			
Unknown	0.42673			(-)			
Unknown	1.666878			(+)			
Unknown	0.801886			(-)			
Unknown	0.724904			(-)			
Unknown	1.291594			(+)			
Unknown	0.84103			(-)			
Unknown	1.577602			(+)			
Unknown	0.695732			(-)			
Unknown	0.863638			(-)			
Unknown	0.648175			(-)			
Unknown	0.802178			(-)			
Unknown	0.740476			(-)			
Unknown	0.700466			(-)			
Unknown	1.210575			(+)			
Unknown	1.350042			(+)			
Unknown		0.009	0.6237	(-)			
Unknown		0.015	1.4949	(+)			
Unknown		0.012	0.7258	(-)			
Unknown		0.002	1.5282	(+)			
Unknown		0.023	0.6626	(-)			
Unknown		0.013	0.789	(-)			
Unknown		0.006	0.6713	(-)			
Unknown		0.002	1.2986	(+)			
Unknown		8E-04	4.6753	(+)			
upregulated during skeletal muscle growth 5		8E-04	0.5704	(-)			
upstream transcription factor 1	0.739612			(-)			
urokinase plasminogen activator receptor	1.496585	0.004	1.3851	(+)	(+)	RCCC	
UUDP glycosyltransferase 1 family, polypeptide A6		8E-04	0.5626	(-)			
vascular cell adhesion molecule 1		8E-04	3.207	(+)	(+)	RCCC	
vascular endothelial growth factor A	0.798289	0.005	0.8443	(-)	(+)	RCCDC	
vascular endothelial zinc finger 1; expressed sequence A1848691	0.923209			(-)			
vasodilator-stimulated	1.377774	0.001	1.7852	(+)			

phosphoprotein						
vitamin D receptor	0.636449			(-)		
v-ral simian leukemia viral oncogene homolog A (ras related)		0.043	1.3333	(+)	(+)	RCCC
v-ral simian leukemia viral oncogene homolog B (ras related)	1.70831	8E-04	1.5091	(+)		
WD repeat domain 1	1.622447			(+)		
Williams-Beuren syndrome chromosome region 14 homolog (human)	0.698155			(-)	(-)	RCCC
WNT1 inducible sigling pathway protein 1		0.003	1.3413	(+)		
X (ictive)-specific transcript, antisense		8E-04	1.5	(+)		
X transporter protein 2		0.038	0.7554	(-)		
Yamaguchi sarcoma viral (v-yes) oncogene homolog		0.03	1.2634	(+)		
Yamaguchi sarcoma viral (v-yes-1) oncogene homolog		0.005	1.4026	(+)	(+)	RCCC
yolk sac gene 2	0.791519			(-)		
zinc finger like protein 1		0.05	0.6885	(-)		
zinc finger protein 144		0.004	1.5968	(+)	(-)	RCCDC
zinc finger protein 36, C3H type-like 1	1.775831	0.001	1.6203	(+)	(+)	RCCC
zinc finger protein 36, C3H type-like 2	2.031905	0.019	1.4281	(+)		
zotuin related factor 2	1.298786			(+)		

Table 16

An ontology analysis in timely dependent fashion: distinct and common ontologies.

The genes in the three phases of renal regeneration and the concordant and discordant genes

- 5 are analyzed for GO (summary sheets). These genes were crossed with the data from supplemental Table 4 (cross sheets); green down-regulated and red up-regulated in RRR.

Gene Category	Up	Down	Genes
<u>cytosolic ribosome (sensu Eukarya)</u>	12	0	RPL29, RPL36A, RPL5, RPL6, SYN1, RPS16, RPS3A, RPS4X, RPS6, RPS7, RPS23, RPL38
<u>carboxylic acid metabolism</u>	3	24	TNFRSF1A, CTPS, ELOVL1, AUH, CPT1A, FAH, FOLR1, GLUL, GPAT, HADHSC, HPD, LPL, MEI, PAH, PKLR, PRODH, SCD, SCP2, SLC7A7, SLC27A2, MLYCD, ACADSB, GATM, CRYL1, CACH-1, MTHFD1, MGC37818
<u>organic acid metabolism</u>	3	24	TNFRSF1A, CTPS, ELOVL1, AUH, CPT1A, FAH, FOLR1, GLUL, GPAT, HADHSC, HPD, LPL, MEI, PAH, PKLR, PRODH, SCD, SCP2, SLC7A7, SLC27A2, MLYCD, ACADSB, GATM, CRYL1, CACH-1, MTHFD1, MGC37818
<u>structural constituent of ribosome</u>	20	0	GADD45A, LAMR1, PTMA, RPL10A, RPL29, RPL36A, RPL5, RPL6, SYN1, RPS16, RPS3A, RPS4X, RPS6, RPS7, RPL27A, RPL3, RPLP1, RPS23, RPL35, RPL38
<u>ribosome</u>	21	0	GADD45A, LAMR1, PTMA, RPL10A, RPL29, RPL36A, RPL5, RPL6, SYN1, RPS16, RPS3A, RPS4X, RPS6, RPS7, RPL27A, RPL3, CTPS, RPLP1, RPS23, RPL35, RPL38

<u>structural molecule activity</u>	36	0	ACTB, ACTG2, ACTG1, ACTA2, CLDN1, CLDN4, COL4A1, COL5A2, CRYM, GADD45A, EMP3, FBNI, KRT8, LAMR1, PTMA, RPL10A, RPL29, RPL36A, RPL5, RPL6, SYNI, RPS16, RPS3A, RPS4X, RPS6, RPS7, TUBA2, RPL27A, RPL3, CLDN7, RPLP1, BAF53A, EFEMP2, RPS23, RPL35, RPL38
<u>fatty acid metabolism</u>	2	12	TNFRSF1A, ELOVL1, CPT1A, GPAT, HADHSC, LPL, PKLR, SCD, SCP2, SLC27A2, MLYCD, ACADSB, CRYL1, CACH-1
<u>ribonucleoprotein complex</u>	25	0	GADD45A, HNRPA1, LAMR1, PTMA, RPL10A, RPL29, RPL36A, RPL5, RPL6, SYNI, RPS16, RPS3A, RPS4X, RPS6, RPS7, RPL27A, RPL3, CTPS, RPLP1, RPS23, RPL35, RPL38, SNRPG, SF3B1, SNRPD2
<u>ribosome biogenesis</u>	10	0	RPL29, RPL36A, RPL5, RPL6, SYNI, RPS16, RPS3A, RPS4X, RPS6, RPS7
<u>ribosome biogenesis and assembly</u>	10	0	RPL29, RPL36A, RPL5, RPL6, SYNI, RPS16, RPS3A, RPS4X, RPS6, RPS7
<u>oxidoreductase activity</u>	7	23	AKR1B10, TXN, YWHAH, GMPR, H3B3, ABP1, DIA1, BCKDHA, CYP2A13, CYP2D6, CYP2J2, DIO1, HADHSC, HPD, MEI, MDH1, NNT, PAH, PRODH, SCD, SOD2, AASS, IVD, ACADSB, CRYL1, DMGDH, ADHS, 061002519Rik, MTHFD1, ALDH7A1
<u>cytoplasm organization and biogenesis</u>	23	2	ACTB, ACTG2, ACTG1, ACTA2, CAPZB, CDC42, CNN2, KRT8, LSP1, TMSB4X, RPL29, RPL36A, RPL5, RPL6, SYNI, RPS16, RPS3A, RPS4X, RPS6, RPS7, TAGLN, TUBA2, CORO1B, ABCD3, SCP2
<u>cytosol</u>	15	6	MTIA, PSME1, RPL29, RPL36A, RPL5, RPL6, SYNI, RPS16, RPS3A, RPS4X, RPS6, RPS7, RPS23, BZW2, RPL38, INPP5B, MEI, MDH1, PKLR, FRAP1, CACH-1
<u>amino acid catabolism</u>	0	6	AUH, FAH, HPD, PAH, PRODH, MGC37818
<u>aromatic compound metabolism</u>	2	6	CTPS, DKFZP434P106, FAH, FOLR1, HPD, PAH, 2010012D11Rik, MTHFD1
<u>amine catabolism</u>	0	6	AUH, FAH, HPD, PAH, PRODH, MGC37818
<u>extracellular space</u>	49	23	ADAM12, BGN, BST1, C1QA, C3, SERPINH1, CD24, CD68, CDH3, CLDN1, CLDN4, COL4A1, COL5A2, CTSS, EDN1, EMP3, ZFP36L1, F3, FBNI, FCER1G, FCGR3A, AKR1B10, GALGT, Gp49a, Gp49b, SCYB10, CYR61, LY6E, MGP, NPDC1, FXDY5, OSMR, PLAUR, PTPRC, SCYA2, CCL9, SPARC, TGFBI, TIMP1, TNC, TNFRSF1A, TYROBP, PLAB, AXL, CLDN7, SLC13A1, PF4, TACSTD2, ABP1, BCKDHA, CYP2J2, DIO1, DNASE1, DPEP1, EGF, F13B, FOLR1, NAPI, KL, Kik1/6, LPL, MEPIA, SLC22A1L, ENPP2, ABCD3, TCN2, VEGF, SLC27A2, TMEM8, DKFZp564K1964.1, CES3, SLC13A3
<u>eukaryotic 43S preinitiation complex</u>	5	0	EIF3S6, RPS4X, RPS6, RPS7, RPS23
<u>physiological process</u>	134	88	ACTB, ACTG2, ACTG1, ACTA2, ADAM12, ADAMTS1, ADSS, ANXA5, ANXA6, ARHB, ARHC, BCL2A1, ARPC2, BST1, ZFP36L1, ZFP36L2, C1QA, C3, CAPZB, SERPINH1, CD24, CD68, CD72, CDC42, SOCS3, CLDN4, CCR2, CNN2, COL5A2, CTSS, GADD45A, EDN1, EIF4EBP1, ELF3, EMP3, F2RL1, F3, FBNI, FCER1G, FCGR3A, AKR1B10, GALGT, GNAI2, GNB2L1, H2-D1, PTPN6, HMGN2, HMGB3, HNRPA1, ICAM1, SCYB10, CYR61, EIF3S6, KRT8, LAMR1, LSP1, LY6E, MGP, MTIA, MYC, BIRC1, NKTR, NPDC1, NPM1, FXDY5, PLAUR, PSME1, PTMA, TMSB4X, PTPRC, RBM3, RPL10A, RPL29, RPL36A, RPL5, RPL6, SYNI, RPS16, RPS3A, RPS4X, RPS6, RPS7, S100A6, SCYA2, CCL9, SCYD1, SPARC, SSR4, TAGLN, TBX6, TSC22, TGFBI, TGIF, TNFRSF1A, TUBA2, TXN, TYROBP, UBE2H, YWHAH, CORO1B, CFDP1, COPEB, AXL, RPL27A, RPL3, CLIC4, H2AFZ, CTPS, ELOVL1, SLC13A1, RPLP1, TCERG1, PTPN9, CSDA, BAF53A, ELF4, PF4, TACSTD2, PMAIP1, EFEMP2, GMPR, RPS23, RPL35, H3B3, BZW2, RPL38, SNRPG, DKFZP434P106, ABP1, SF3B1, UBE2N, SNRPD2, DIA1, CLIC1, Ak4, AUH, BCKDHA, CALB1, CPT1A, CYP2A13, CYP2D6, CYP2J2, DIO1, DNASE1, DPEP1, EGF, F13B, FAH, FOLR1, G6PC, GAS2, GGT1, GLUL, GPAT, GK, HADHSC, HPD, HPN, INPP5B, NAPI, KHK, KL, BTEB1, Kik1/6, Kik26, LPL, MEPIA, MEI, MDH1, MUT, NNT, SLC22A1L, PAH, ENPP2, PKLR, PAPOLA, ILF, PRODH, ABCD3, SLC22A8, SCD, SCP2, SLC22A1, SLC22A2, SLC22A5, SLC7A7, SOD2, TCN2, THRSP, VEGF, SLC26A4, SLC27A2, RPC5, SGK2, JDP1, AASS, SLC7A9, USP2, FLC4A4, PGAM2, IVD, MLYCD, FRAP1, HERPUD1, OSBP1A, KLF15, FLJ10241, ACADSB, GATM, FLJ13448, 2010012D11Rik, MGC15416, CRYL1,

DMGDH, CACH-1, ADH8, 0610025119Rik, SLC17A3, MTHFD1,  
ALDH7A1, SLC13A3, MGC37818

<u>blood coagulation</u>	6	2	ANXA5, ANXA6, F2RL1, F3, PF4, EFEMP2, F13B, MGC15416
<u>response to external stimulus</u>	30	6	ACTG1, BST1, C1QA, C3, SERPINH1, CD24, CD72, CCR2, FBN1, FCER1G, FCGR3A, GNAI2, H2-D1, ICAM1, SCYB10, CYR61, LSP1, LY6E, PSME1, PTMA, PTPRC, SCYA2, CCL9, SCYD1, TNFRSF1A, TYROBP, COPEB, PF4, TACSTD2, ABP1, SLC22A1L, SOD2, SLC26A4, HERPUD1, OSBP1A, ALDH7A1
<u>eukaryotic 48S initiation complex</u>	4	0	RPS4X, RPS6, RPS7, RPS23
<u>cytosolic small ribosomal subunit (sensu Eukarya)</u>	4	0	RPS4X, RPS6, RPS7, RPS23
<u>hemostasis</u>	6	2	ANXA5, ANXA6, F2RL1, F3, PF4, EFEMP2, F13B, MGC15416
<u>extracellular</u>	54	23	ADAM12, ADAMTS1, BGN, BST1, C1QA, C3, SERPINH1, CD24, CD68, CDH3, CLDN1, CLDN4, COL4A1, COL5A2, CSTB, CTSS, EDN1, EMP3, F2RL1, F3, FBN1, FCER1G, FCGR3A, AKR1B10, GALGT, Gp49a, Gp49b, SCYB10, CYR61, LY6E, MGP, NPDC1, FXDY5, OSMR, PLAUR, PTPRC, SCYA2, CCL9, SCYD1, SPARC, TGFB1, TIMP1, TNC, TNFRSF1A, TYROBP, CFDP1, PLAB, AXL, CLDN7, SLC13A1, PF4, TACSTD2, EFEMP2, ABP1, BCKDHA, CYP2J2, DIO1, DNASE1, DPEP1, EGF, F13B, FOLR1, NAPI, KL, Kik1/6, LPL, MEPIA, SLC22A1L, ENPP2, ABCD3, TCN2, VEGF, SLC27A2, TMEM8, DKFpZp564K1964.1, CES3, SLC13A3
<u>biosynthesis</u>	24	11	ADSS, GADD45A, EIF4EBP1, EIF3S6, LAMR1, RPL10A, RPL29, RPL36A, RPL5, RPL6, RPS16, RPS3A, RPS4X, RPS6, RPS7, RPL27A, RPL3, CTPS, ELOVL1, RPLP1, RPS23, RPL35, BZW2, RPL38, G6PC, GGT1, GLUL, GPAT, FAH, PKLR, PRODH, SCD, MLYCD, GATM, MTHFD1
<u>cell organization and biogenesis</u>	26	2	ACTB, ACTG2, ACTG1, ACTA2, CAPZB, CDC42, CNN2, KRT8, LSP1, TMSB4X, RPL29, RPL36A, RPL5, RPL6, SYNI, RPS16, RPS3A, RPS4X, RPS6, RPS7, TAGLN, TUBA2, CORO1B, CFDP1, HZAFZ, BAF53A, ABCD3, SCP2
<u>response to abiotic stimulus</u>	12	4	ACTG1, SERPINH1, CCR2, FBN1, GNAI2, SCYB10, CYR61, LSP1, SCYA2, CCL9, PF4, ABP1, SLC22A1L, SLC26A4, OSBP1A, ALDH7A1
<u>protein biosynthesis</u>	21	0	GADD45A, EIF4EBP1, EIF3S6, LAMR1, RPL10A, RPL29, RPL36A, RPL5, RPL6, RPS3A, RPS4X, RPS6, RPS7, RPL27A, RPL3, RPLP1, RPS23, RPL35, BZW2, RPL38
<u>actin binding</u>	8	3	CAPZB, CNN2, LSP1, TMSB4X, TAGLN, VASP, CORO1B, TPM3, DNASE1, TLN2, SLC13A3
<u>posttranslational membrane targeting</u>	4	3	BST1, CD24, LY6E, PLAUR, DPEP1, FOLR1, LPL
<u>macromolecule biosynthesis</u>	24	6	ADSS, GADD45A, EIF4EBP1, EIF3S6, LAMR1, RPL10A, RPL29, RPL36A, RPL5, RPL6, RPS3A, RPS4X, RPS6, RPS7, RPL27A, RPL3, CTPS, ELOVL1, RPLP1, RPS23, RPL35, BZW2, RPL38, G6PC, GPAT, PKLR, SCD, MLYCD, MTHFD1
<u>small ribosomal subunit</u>	5	0	LAMR1, RPS4X, RPS6, RPS7, RPS23
<u>L-phenylalanine metabolism</u>	0	3	FAH, HPD, PAH

<u>phenylalanine catabolism</u>	0	3	FAH, HPD, PAH
<u>RNA binding</u>	17	2	HNRPA1, NPM1, RBM3, RPL5, RPS16, RPS3A, RPS4X, RPS6, RPS7, RPL27A, RPL3, RPLP1, RPS23, RPL38, SNRPG, SE3B1, SNRPD2, AUH, PAPOLA
<u>mitochondrion</u>	3	22	CLIC4, PMAIP1, H3B3b, Ak4, AUH, BCKDHA, CPT1A, GLUL, GPAT, GK, HADHSC, KHK, MUT, NNT, PRODH, SCP2, SOD2, IVD, MLYCD, FLJ10241, ACADSB, GATM, FLJ13448, DMGDH, 0610025I19Rik
<u>amino acid and derivative metabolism</u>	1	11	CTPS, AUH, DIO1, FAH, GLUL, HPD, PAH, PRODH, SLC7A7, GATM, MTHFD1, MGC37818
<u>response to chemical substance</u>	9	1	CCR2, GNAI2, SCYB10, CYR61, LSP1, SCYA2, CCL9, PF4, ABP1, SLC22A1L
<u>anion transporter activity</u>	1	4	SLC13A1, SLC22A1L, SLC26A4, SLC4A4, SLC13A3
<u>aromatic amino acid family catabolism</u>	0	3	FAH, HPD, PAH
<u>aromatic compound catabolism</u>	0	3	FAH, HPD, PAH
<u>amino acid metabolism</u>	1	9	CTPS, AUH, FAH, GLUL, HPD, PAH, PRODH, SLC7A7, MTHFD1, MGC37818
<u>protein-ER targeting</u>	4	3	BST1, CD24, LY6E, PLAUR, DPEP1, FOLR1, LPL
<u>anion transport</u>	3	4	CLIC4, SLC13A1, CLIC1, SLC22A1L, SLC26A4, SLC4A4, SLC13A3
<u>protein-membrane targeting</u>	4	3	BST1, CD24, LY6E, PLAUR, DPEP1, FOLR1, LPL
<u>inorganic anion transport</u>	3	2	CLIC4, SLC13A1, CLIC1, SLC26A4, SLC4A4
<u>response to biotic stimulus</u>	24	2	BST1, CIQA, C3, CD24, CD72, CCR2, FCER1G, FCGR3A, H2-D1, ICAM1, SCYB10, LSP1, LY6E, PSME1, PTMA, PTPRC, SCYA2, CCL9, SCYD1, TNFRSF1A, TYROBP, COPEB, PF4, TACSTD2, SOD2, HERPUD1
<u>actin filament</u>	3	1	ACTG2, ACTG1, BAF53A, GAS2
<u>immunoglobulin binding</u>	3	0	FCER1G, FCGR3A, LGALS3
<u>ion transporter activity</u>	2	10	SLC13A1, H3B3b, NNT, SLC22A1L, SLC22A8, SLC22A1, SLC22A2, SLC22A5, TCN2, SLC26A4, SLC4A4, SLC13A3
<u>chemotaxis</u>	7	0	CCR2, SCYB10, CYR61, LSP1, SCYA2, CCL9, PF4
<u>taxis</u>	7	0	CCR2, SCYB10, CYR61, LSP1, SCYA2, CCL9, PF4
<u>defense response</u>	24	0	BST1, CIQA, C3, CD24, CD72, CCR2, FCER1G, FCGR3A, H2-D1, ICAM1, SCYB10, LSP1, LY6E, PSME1, PTMA, PTPRC, SCYA2, CCL9, SCYD1, TNFRSF1A, TYROBP, COPEB, PF4, TACSTD2
<u>chemokine receptor binding</u>	5	0	SCYB10, SCYA2, CCL9, SCYD1, PF4
<u>G-protein-coupled receptor binding</u>	5	0	SCYB10, SCYA2, CCL9, SCYD1, PF4
<u>chemokine activity</u>	5	0	SCYB10, SCYA2, CCL9, SCYD1, PF4
<u>heparin binding</u>	4	2	ADAMTS1, CYR61, PF4, ABP1, LPL, VEGF
<u>amine metabolism</u>	1	11	CTPS, AUH, DIO1, FAH, GLUL, HPD, PAH, PRODH, SLC7A7, GATM, MTHFD1, MGC37818



**Table 17.** The differently expressed genes in both RRR and RCC exhibited distinct ontologies for the concordance vs. discordance genes. The differentially expressed genes in both RRR and RCC were clustered according to their concordance vs. discordant change.

- 5 Functional ontology was analysis performed ( $p < 0.05$ ). The ontologies are hyperlinked to EMBL-EBI. The average RRR expression of each ontology is presented in a green to red scale; green down-regulated, red up-regulated. The number and average RRR expression of genes up- / down- regulated in both RRR and RCC, the category p-value and enrichment are also given (the expression direction and values is as in RRR relative to the normal kidney).

Category	Concordant					p<0.05
	Average Expression	Total Expression UP	No Genes-UP	Total Expression DOWN	No Genes-DOWN	
<u>immunoglobulin binding</u>	1.103	3.3092367	3	0	0	0.0340422
<u>extracellular matrix structural constituent conferring tensile strength</u>	0.884	4.4205293	5	0	0	0.0140517
<u>structural constituent of ribosome</u>	0.741	17.785127	24	0	0	4.242E-10
<u>extracellular matrix structural constituent</u>	0.801	4.8043204	6	0	0	0.0423389
<u>RNA binding</u>	0.564	16.226181	27	1	-0.436683	3.91E-06
<u>structural molecule activity</u>	0.762	30.582787	38	1	-0.85197	1.933E-07
<u>nucleic acid binding</u>	0.488	36.804271	64	5	-3.163539	0.0199209
<u>cytosolic ribosome (sensu Eukarya)</u>	0.732	8.0487542	11	0	0	3.447E-07
<u>proteasome core complex (sensu Eukarya)</u>	0.564	2.2564559	4	0	0	0.0304081
<u>eukaryotic 43S preinitiation complex</u>	0.529	2.1141753	4	0	0	0.036631
<u>small ribosomal subunit</u>	0.701	3.5057175	5	0	0	0.0160654
<u>collagen</u>	0.884	4.4205293	5	0	0	0.0160654
<u>proteasome complex (sensu Eukarya)</u>	0.521	2.6060329	5	0	0	0.0301159
<u>basement membrane</u>	0.929	5.5744617	6	0	0	0.0136794
<u>ribosome</u>	0.738	16.964075	23	0	0	1.114E-07
<u>ribonucleoprotein complex</u>	0.687	20.599567	30	0	0	5.336E-08
<u>chromatin</u>	0.541	5.3809737	7	1	-1.049901	0.0322996
<u>cytosol</u>	0.603	14.450534	21	2	-0.584947	0.0003098
<u>extracellular matrix</u>	0.799	11.577839	13	1	-0.393003	0.0361871
<u>L-phenylalanine metabolism</u>	-1.203	0	0	3	-3.608402	0.015339
<u>phenylalanine catabolism</u>	-1.203	0	0	3	-3.608402	0.015339
<u>aromatic amino acid family catabolism</u>	-1.203	0	0	3	-3.608402	0.0246852
<u>aromatic compound catabolism</u>	-1.203	0	0	3	-3.608402	0.0246852
<u>tyrosine metabolism</u>	-1.033	0	0	3	-3.099756	0.0246852
<u>DNA replication initiation</u>	0.609	3.0432735	5	0	0	0.0018226

aromatic amino acid family metabolism	-1.037	0	0	4	-4.149657	0.0094724
ribosome biogenesis	0.752	7.5160166	10	0	0	0.0001702
regulation of translation	0.137	1.8846141	4	2	-1.063299	0.0071406
ribosome biogenesis and assembly	0.752	7.5160166	10	0	0	0.0002083
DNA dependent DNA replication	0.546	3.2738639	6	0	0	0.0139176
aromatic compound metabolism	-0.503	1.5973586	1	6	-5.120159	0.013176
posttranslational membrane targeting	0.491	4.7069693	5	2	-1.272969	0.013176
protein-ER targeting	0.481	5.1236426	6	2	-1.272969	0.0072796
protein-membrane targeting	0.491	4.7069693	5	2	-1.272969	0.0259582
protein biosynthesis	0.610	18.130535	26	2	-1.063299	2.836E-05
translation	0.372	4.7791123	8	2	-1.063299	0.0249621
response to pest/pathogen/parasite	0.938	13.132262	14	0	0	0.0397381
biosynthesis	0.360	19.843752	30	9	-5.785595	0.0008202
cell adhesion	0.672	15.366891	19	2	-1.244973	0.0217328
macromolecule biosynthesis	0.560	19.256841	29	3	-1.323209	0.0041806
immune response	0.912	19.157513	21	0	0	0.0255412
cell organization and biogenesis	0.697	20.530417	26	2	-1.015958	0.0098063
defense response	0.859	21.468511	25	0	0	0.0220773
response to biotic stimulus	0.843	21.929029	26	0	0	0.0324375
response to external stimulus	0.763	24.757761	31	1	-0.33857	0.051035
cell proliferation	0.517	18.235487	33	1	-0.661095	0.0479313
protein metabolism	0.466	41.656205	60	10	-9.069116	0.0221394
physiological process	0.333	113.38449	167	52	-40.53305	0.0152323
carboxylic acid metabolism	-0.547	0.8960719	2	15	-10.20242	0.0128196
organic acid metabolism	-0.547	0.8960719	2	15	-10.20242	0.0135279
cytoplasm organization and biogenesis	0.747	17.44005	20	2	-1.015958	0.0113533
cell growth and/or maintenance	0.325	52.152783	78	25	-18.64241	0.0032613

Category	Discordant				
	Total Expression UP	No Genes-UP	Total Expression DOWN	No Genes-DOWN	p<0.05
carboxylic acid metabolism	0	0	-5.598769	8	0.0151991
organic acid metabolism	0	0	-5.598769	8	0.015667
cytoplasm organization and biogenesis	2.4955781	5	-1.5467431	4	0.0315753
cell growth and/or maintenance	7.3648921	13	-11.551056	20	0.0450794
insulin-like growth factor binding	1.7450831	2	-1.3912086	2	0.0006866
organic cation transporter activity	0.3754932	1	-1.1781775	2	0.0161759
growth factor binding	1.7450831	2	-1.3912086	2	0.0027999
heparin binding	3.3125522	4	-1.7921275	2	0.0002486
glycosaminoglycan binding	3.3125522	4	-1.7921275	2	0.0005008
cation transporter activity	0.3754932	1	-2.6061538	4	0.0466136
catalytic activity	3.9243146	9	-16.911395	30	0.0306027
extracellular space	9.491228	12	-7.4596714	12	0.0395413
regulation of axon extension	0.7769723	1	-0.3395731	1	0.0617602
one-carbon compound metabolism	0	0	-1.5503316	3	0.0287613
angiogenesis	2.53558	3	-0.5766978	2	0.0023126
regulation of cell growth	1.7450831	2	-1.3912086	2	0.0113371

blood vessel development	2.53558	3	-0.5766978	2	0.0037461
cell growth	1.7450831	2	-1.8333907	3	0.0044579
cytoskeleton organization and biogenesis	2.4955781	5	-0.9460864	3	0.0110569
regulation of cellular process	1.7450831	2	-2.4914104	4	0.0379138
regulation of biological process	1.7450831	2	-2.4914104	4	0.0391032
organelle organization and biogenesis	2.4955781	5	-1.5467431	4	0.0108806
organogenesis	6.7050688	8	-2.696574	6	0.030497
anorphogenesis	6.7050688	8	-2.696574	6	0.0489539



VHL pathway	104	59	0	16	0.0001	29	0	28	0.609	50	0.978	26	0.528	85	<0.00	19	<0.00
Hypoxia pathway	95	35	0.000	16	<0.00	44	<0.00	24	0.932	50	0.347	21	0.214	63	0.276	32	0.276
HRE target (HIF)	17	4	0.968	7	<0.00	6	0.001	2	0.349	12	0.093	3	0.485	10	0.916	7	0.916
IGF pathway	37	9	0.762	8	0.0003	20	0.016	10	0.852	19	0.754	8	0.477	25	0.472	12	0.472
Myc pathway	136	55	<0.00	10	0.714	71	<0.00	39	0.259	61	0.578	36	0.719	113	<0.00	23	<0.00
p53 pathway	262	80	<0.00	32	<0.00	150	<0.00	69	0.456	11	0.100	81	0.300	199	<0.00	63	<0.00
NF- $\kappa$ B pathway	52	19	0.008	5	0.4681	28	0.003	19	0.054	21	0.366	12	0.501	43	0.001	9	0.001

**Table 19.** The RRR genes in non-probabilistic GO ontologies. The comprehensive probabilistic analysis may fail to capture many key aspects of the concordant and discordant gene functions. Therefore, we also categorized the genes into gene-by-gene, non-probabilistic GO.

Gene symbol	Gene name	RRR/Normal	RCC/Normal	Molecular Function
TJP2	tight junction protein 2	Up	Down	Guanylate kinase activity
HAKS	histidyl R synthetase	Down	Up	Histidine-RNA ligase activity; ATP binding
IF	complement component factor i	Up	Down	Scavenger receptor activity; Trypsin activity
CYR61/IGFBP10	cysteine rich protein 61	Up	Down	Heparin binding; Insulin-like growth factor binding
FHIT	fragile histidine triad gene	Up	Down	Magnesium ion binding; Manganese ion binding; Bis(S'-adenosyl)-triphosphatase activity; Hydrolase activity
APOE	apolipoprotein E	Up	Down	Tau protein binding; Lipid binding; Lipid transporter activity; Antioxidant activity; Heparin binding; Apolipoprotein E receptor binding; Beta-amyloid binding

EGln1	EGln nine homolog 1 (C. elegans)	Down	Up	Oxidoreductase activity; Oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, 2-oxoglutarate as one donor, and incorporation of one atom each of oxygen into both donors; Oxidoreductase activity, acting on single donors with incorporation of molecular oxygen, incorporation of two atoms of oxygen
CEACAM1	CEA-related cell adhesion molecule 1	Down	Up	Molecular_function unknown
MT2A	metallothionein 2	Up	Down	Copper ion binding; Metal ion binding
LPL	lipoprotein lipase	Down	Up	Heparin binding; Hydrolase activity; Lipid transporter activity; Lipoprotein lipase activity
TACSTD2	tumor-associated calcium signal transducer 2	Up	Down	Receptor activity
PLAT	plasminogen activator, tissue	Up	Down	Peptidase activity; Plasminogen activator activity; Trypsin activity; Chymotrypsin activity; Hydrolase activity
C16orf5	RIKEN cd 5730403B10 gene	Down	Up	Molecular_function unknown
EIF4A2	eukaryotic translation initiation factor 4A2	Down	Up	ATP binding; Translation initiation factor activity; ATP-dependent helicase activity; DNA binding; RNA binding; Hydrolase activity; Nucleic acid binding
TCF21	transcription factor 21	Up	Down	DNA binding; RNA polymerase II transcription factor activity
RALBP1	Ral-interacting protein 1	Up	Down	GTPase activator activity
HSPD1	heat shock protein 1 (chaperonin) / heat shock protein, 60 kDa	Down	Up	Unfolded protein binding; ATP binding
SCP2	sterol carrier protein 2, liver	Down	Up	Sterol carrier activity; Lipid binding

CTGF/ IGFBP8	connective tissue growth factor	Up	Down	Protein binding; Heparin binding; Insulin-like growth factor binding
CPT1A	carnitine palmitoyltransferase 1, liver	Down	Up	Transferase activity; Acyltransferase activity; Carnitine O-palmitoyltransferase activity
PGK1	phosphoglycerate kinase 1	Down	Up	Phosphoglycerate kinase activity; Transferase activity
GC	group specific component	Up	Down	Actin binding; Carrier activity; Vitamin D binding
HK1	hexokinase 1	Down	Up	ATP binding; Kinase activity; Hexokinase activity; Transferase activity
DCN	decorin	Up	Down	(?)
TOP2B	topoisomerase (D) III beta	Down	Up	DNA topoisomerase type I activity;
FRAP1	FK506 binding protein 12-rapamycin associated protein 1	Down	Up	Transferase activity; Binding; Inositol or phosphatidylinositol kinase activity
IGFBP1	insulin-like growth factor binding protein 1	Down	Up	Insulin-like growth factor binding
RITN3	reticulon 3	Down	Up	Molecular_function unknown
TM4SF3	Mus musculus, clone MGC:38563 IMAGE:5344986, mRNA, complete cds	Up	Down	Signal transducer activity
GPC3	glypican 3	Up	Down	(?)
NR2F6	nuclear receptor subfamily 2, group F, member 6	Up	Down	Thyroid hormone receptor activity; Steroid hormone receptor activity; Transcription factor activity
ZNF144	zinc finger protein 144	Up	Down	Transcription factor activity; Ubiquitin-protein ligase activity; Zinc ion binding



SLC1A1	solute carrier family 1, member 1	Up	Down	Sodium/dicarboxylate symporter activity; Symporter activity; L-glutamate transporter activity
SDC1	syndecan 1	Up	Down	Cytoskeletal protein binding
BCKDHA	branched chain ketoacid dehydrogenase E1, alpha polypeptide	Down	Up	3-methyl-2-oxobutanoate dehydrogenase (2-methylpropanoyl)-transfering activity; Alpha-ketoad dehydrogenase activity; Oxidoreductase activity; Oxidoreductase activity, acting on the aldehyde or oxo group of donors, disulfide as acceptor
SOD2	superoxide dismutase 2, mitochondrial	Down	Up	Oxidoreductase activity; Superoxide dismutase activity; Manganese ion binding; Manganese superoxide dismutase activity; Metal ion binding
SMC1L1	SMC (structural maintenance of chromosomes 1)-like 1 (S. cerevisiae)	Up	Down	Chromatin binding; Protein binding; ATP binding; Protein heterodimerization activity; ATPase activity; Microtubule motor activity
GRSF1	G-rich RNA sequence binding factor 1 (DSWsu31e) D segment, Chr 5, Wayne State University 31, expressed	Down	Up	mRNA binding
AMACR	alpha-methylacyl-CoA racemase	Down	Up	Catalytic activity; Isomerase activity; Alpha-methylacyl-CoA racemase activity
ENPP2	ectonucleotide pyrophosphatase/phosphodiesterase 2	Down	Up	Phosphodiesterase 1 activity; Transcription factor binding; Endonuclease activity; Hydrolase activity; Nucleic acid binding; Nucleotide diphosphatase activity

PCTK3	PCTAIRE-motif protein kase 3	Down	Up	Signal transducer activity; ATP binding; Transferase activity; Protein serine/threonine kinase activity; Protein-tyrosine kinase activity
		Down	Up	
NCOA4	nuclear receptor coactivator 4	Down	Up	Transcription coactivator activity
KDR	kase insert domain protein receptor	Down	Up	Receptor activity; Transferase activity; Vascular endothelial growth factor receptor activity; ATP binding
CORO1B	coronin, actin binding protein 1B	Up	Down	Actin binding
WSB1	RIKEN cd 270003M07 gene - pending	Up	Down	Molecular_function unknown
KIAA1049	RIKEN cd 1100001J13 gene - pending	Down	Up	(?)
SLC16A7	solute carrier family 16 (monocarboxylic acid transporters), member 7	Down	Up	Transporter activity; Monocarboxylate porter activity; Pyruvate carrier activity; Symporter activity
IGFBP3	insulin-like growth factor binding protein 3	Down	Up	Insulin-like growth factor binding; Insulin-like growth factor binding; Metal ion binding; Protein tyrosine phosphatase activator activity
MMP2	matrix metalloproteinase 2	Up	Down/Possible Conflict	Calcium ion binding; Gelatinase A activity; Hydrolase activity; Zinc ion binding
MTHFD1	methylenetetrahydrofolate dehydrogenase (DP+ dependent), methylenetetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthase	Down	Up	Oxidoreductase activity; Hydrolase activity; Ligase activity; Methylenetetrahydrofolate cyclohydrolase activity; ATP binding; Methylenetetrahydrofolate dehydrogenase (NADP+) activity; Formate-tetrahydrofolate ligase activity
PKD1	polycystic kidney disease 1 homolog	Down	Up	Sugar binding

MAT7A	Mus musculus, clone MGC:6545 IMAGE:2655444, mt, complete cds	Down	Up	ATP binding; Magnesium ion binding; Methionine adenosyltransferase activity; Transferase activity
SHMT2	serine hydroxymethyl transferase 2 (mitochondrial); RUKEN cD 2700043D08 gene	Down	Up	Transferase activity; Glycine hydroxymethyltransferase activity
PHL1	four and a half LIM domains 1	Down	Up	Zinc ion binding
VEGF	vascular endothelial growth factor A	Down	Up	Heparin binding; Vascular endothelial growth factor receptor binding; Extracellular matrix binding; Growth factor activity; protein homodimerization activity
PAFOLA	poly (A) polymerase alpha	Down	Up	Polynucleotide adenylyltransferase activity; Transferase activity; RNA binding
MYL6	myosin light chain, alkali, nonmuscle	Up	Down	Calcium ion binding
SHMT1	serine hydroxymethyl transferase 1 (soluble)	Down	Up	Glycine hydroxymethyltransferase activity; Transferase activity
GJB2	gap junction membrane channel protein beta 2	Down	Up	Connexon channel activity
HSPH1	heat shock protein, 105 kDa	Down	Up	ATP binding
PTPRB	protein tyrosine phosphatase, receptor type, B	Down	Up	Hydrolase activity; Transmembrane receptor protein tyrosine phosphatase activity
UBE2V1	Mus musculus, Similar to ubiquitin-conjugating enzyme E2 variant 1, clone MGC:7660 IMAGE:3496083, mt, complete cds	Down	Up	Transcriptional activator activity; Ubiquitin conjugating enzyme activity

KIF21A	kinesin family member 21A	Down	Up	ATP binding; Motor activity
THBS1	thrombospondin 1	Up	Down	Protein binding; Signal transducer activity; Calcium ion binding; Structural molecule activity; Endopeptidase inhibitor activity; Heparin binding
MKNK2	G protein-coupled receptor like 7	Down	Up	ATP binding; Transferase activity; Protein-serine/threonine kinase activity; Protein-tyrosine kinase activity
ADD3	adducin 3 (gamma)	Down	Up	Calmodulin binding; Structural constituent of cytoskeleton
Klk1	kallikrein 6	Down	Up	Chymotrypsin activity; Peptidase activity; Tissue kallikrein activity; Trypsin activity
ATP1B1	ATPase, $H^{+}/K^{+}$ transporting, beta 1 polypeptide	Down	Up	Sodium:potassium-exchanging ATPase activity;
ARHE	ras homolog gene family, member E	Down	Up	GTP binding
PTPRO	protein tyrosine phosphatase, receptor type, O	Up	Down	Protein tyrosine phosphatase activity; Protein tyrosine phosphatase activity; Receptor activity; Transmembrane receptor protein tyrosine phosphatase activity; Hydrolase activity
MEP1A	meprin 1 alpha	Down	Up	Meprin A activity; Metalloproteinase activity; Asparaginase activity; Zinc ion binding; Hydrolase activity
COX6C	cytochrome c oxidase, subunit VIc	Down	Up	Cytochrome-c oxidase activity; Oxidoreductase activity
SLC22A1	solute carrier family 22 (organic cation transporter), member 1	Down	Up	Ion transporter activity; Organic cation transporter activity; ATP binding

SPTLC1	Serine palmitoyltransferase, long chain base subunit 1	Down	Up	Serine C-palmitoyltransferase activity; Transferase activity; Acyltransferase activity
CAPNS1	calpain, small subunit 1	Down	Up	Calcium ion binding; Calpain activity
RRM1	ribonucleotide reductase M1	Down	Up	Oxidoreductase activity; Ribonucleoside-diphosphate reductase activity
SAR1	SAR1 a gene homolog (S. cerevisiae)	Up	Down	GTP binding;
PPP2CB	protein phosphatase 2a, catalytic subunit, beta isoform	Up	Down	Phosphoprotein phosphatase activity; Protein phosphatase type 2A activity; Hydrolase activity; Manganese ion binding
AKAP2	A kinase (PRK\A) anchor protein 2	Up	Down	Kinase activity; Protein kinase A binding
ACOX1	acyl-Coenzyme A oxidase 1, palmitoyl	Down	Up	Oxidoreductase activity; Acyl-CoA oxidase activity; Electron donor activity
CD59	CD59a antigen	Down	Up	(?)
CRYM	crystallin, mu	Up	Down	Ornithine cyclodeaminase activity
GADD45G	growth arrest and D-damage-inducible 45 gamma	Down	Up/ Possible Conflict	(?)

**Table 20.** An ontology analysis of the concordant and discordant genes in pathway dependent fashion: distinct and common ontologies. The concordantly and discordantly differentially expressed genes were clustered according to their regulation by the pathways of VHL, hypoxia, HIF, IGF1, MYC, p53 and NF- $\kappa$ B. Functional ontology was analysis performed ( $p < 0.05$ ).

Ontology	Concordant	Discordant
enzyme inhibitor activity	HYPOXIA	
cytosol	HYPOXIA, MYC	
structural molecule activity	VHL, HYPOXIA, MYC, p53	
protein biosynthesis	VHL, HYPOXIA, MYC	
ribosome	VHL, HYPOXIA, MYC	
structural constituent of ribosome	VHL, HYPOXIA, MYC	
cell proliferation	VHL, MYC, p53	
cell growth and/or maintenance	VHL, MYC, p53	
DNA dependent DNA replication	VHL, MYC, p53	
DNA replication initiation	VHL, p53	
collagen type V	VHL	
cell organization and biogenesis	MYC	
ribosome biogenesis and assembly	MYC	
intracellular	MYC	
binding	MYC	
regulation of cell cycle	MYC, p53	
response to stress	p53	
cell communication	p53	
intracellular signaling cascade	p53	
protein targeting	p53	
DNA dependent ATPase activity	p53	
protein binding	p53	
cell adhesion	NF $\kappa$ B	
secretory pathway	NF $\kappa$ B	
plasma membrane	NF $\kappa$ B	
immune response	p53, NF $\kappa$ B	
death	p53, NF $\kappa$ B	
posttranslational membrane targeting	p53, NF $\kappa$ B	
protein-ER targeting	p53, NF $\kappa$ B	
signal transducer activity	p53	IGF1
extracellular	NF $\kappa$ B	IGF1
protein metabolism	VHL, HYPOXIA, MYC	VHL
glycolysis		HIF

regulation of cell growth		HIF, IGF
cell growth		HYPOXIA
insulin-like growth factor binding		HYPOXIA, HIF, IGF1
extracellular space		IGF1
receptor activity		IGF1
one-carbon compound metabolism		p53
angiogenesis		p53, IGF1
morphogenesis/ organogenesis		p53, IGF1
heparin binding		p53, IGF1
ATP binding		VHL
response to heat		VHL, p53

A number of embodiments of the invention have been described. Nevertheless, it will be understood that various modifications may be made without departing from the spirit and scope of the invention. Accordingly, other embodiments are within the scope of the following claims.

All publications and patent documents cited in this application are incorporated by reference in their entirety for all purposes to the same extent as if each individual publication or patent document were so individually denoted. By their citation of various references in this document, Applicants do not admit any particular reference is "prior art" to their invention.

What is claimed is:

1. A method of qualifying the tissue status in a subject comprising:

(a) measuring at least one biomarker in a sample from the subject, wherein the biomarker is selected from the group consisting of the markers listed in Table 9; and

(b) correlating the measurement with tissue status.

2. The method of claim 1, further comprising:

(c) managing treatment of the subject based on the status.

3. The method of claim 2, wherein managing treatment is selected from ordering more tests, performing surgery, chemotherapy, dialysis, treatment of acute organ failure, organ transplantation, wound healing treatment, and taking no further action.

4. The method of claim 2, further comprising:

(d) measuring the at least one biomarker after subject management.

5. The method of claim 1, wherein the tissue status is selected from the group consisting of the subject's risk of cancer, regeneration, tissue repair, acute organ failure, organ transplantation, the presence or absence of disease, the stage of disease and the effectiveness of treatment of disease.

6. The method of claim 5, further comprising measuring at least two biomarkers in a sample from the subject and correlating measurement of the biomarkers with renal status.

7. The method of claim 1, wherein the biomarkers are selected from Table 9.

8. The method of claim 1 wherein the biomarkers are selected from any one or more of Cluster 1 – 27.

9. The method of claim 1, wherein the biomarkers are selected from any one or more of discordant genes.

10. The method of claim 1, wherein the biomarkers are selected from any one or more of concordant genes.

11. The method of any one of claim 1, wherein measuring comprises:

(a) providing a nucleic acid sample from the subject; and

(c) capturing one or more of the biomarkers on a surface of a substrate comprising capture reagents that bind the biomarkers.



12. The method of claim 11, wherein the substrate is a nucleic acid chip.
13. The method of claim 12, wherein the nucleic acid chip is an RNA or DNA chip.
14. The method of claim 11, wherein the substrate is a microtiter plate comprising biospecific affinity reagents that bind the at least one biomarkers and wherein the biomarkers are detected by fluorescent labels.
15. The method of claim 11, wherein the nucleic acid sample from a subject is labeled.
16. The method of claim 1, wherein measuring is selected from detecting the presence or absence of the biomarkers(s), quantifying the amount of marker(s), and qualifying the type of biomarker.
17. The method of claim 1, wherein at least one biomarker is measured using a biochip array.
18. The method of claim 17, wherein the biochip array is an antibody chip array, tissue chip array, protein chip array, or a peptide chip array.
19. The method of claim 17, wherein the biochip array is a nucleic acid array.
20. The method of claim 17, wherein at least one biomarker capture reagent is immobilized on the biochip array.
21. The method of claim 1, wherein the protein biomarkers are measured by immunoassay.
22. The method of claim 1, wherein the correlating is performed by a software classification algorithm.
23. The method of claim 1 wherein the sample is selected from one or more of blood, serum, kidney, renal tumor, renal cyst, renal metastasis, kidney cell or cells, kidney tissue, plasma, urine, saliva, and feces.
24. The method of claim 1, wherein the tissue is kidney, liver, lung, heart, or skin.
25. A method of diagnosing renal status in a subject, comprising:  
determining the pattern of expression of one or more markers listed in Table 9 in a sample from the subject, wherein a differential expression pattern of the one or more markers in a subject is indicative of cancer.
26. The method of claim 1 25, wherein the determining is of any one or more of Trends 1

- 27.

27. The method of claim 25, wherein the determining is of any one or more of clusters 1 – 27.
28. The method of claim 25, wherein the sample from the subject is selected from one or more of a kidney cell or cells, kidney tissue or blood cell.
- 5 29. A method comprising measuring a plurality of biomarkers in a sample from the subject, wherein the biomarkers are selected from one or more of the group consisting of Table 9 or Clusters 1 – 27.
30. A kit comprising:
  - (a) a capture reagent that binds a biomarker selected from Table 9 or Cluster 1 – 27  
0 and combinations thereof; and
  - (b) a container comprising at least one of the biomarkers.
31. The kit of claim 30, wherein the capture reagent binds a plurality of the biomarkers.
32. The kit of any one of claims 30 – 31, wherein the capture reagent is a nucleic acid probe.
- 5 33. The kit of any one of claims 30 – 31, further comprising a second capture reagent that binds one of the biomarkers that the first capture reagent does not bind.
34. A kit comprising a plurality of capture reagents that binds one or more biomarkers selected from Table 9 or Cluster 1 – 27.
35. The kit of claim 34, wherein the at least one capture reagent is an antibody or a nucleic  
) acid complementary to the biomarker.
36. The kit of any one of claims 34 – 35, further comprising a wash solution that selectively allows retention of the bound biomarker to the capture reagent as compared with other biomarkers after washing.
37. The kit of claim 36, further comprising instructions for using the capture reagent to detect the biomarker.
38. The kit of any one of claims 37, further comprising written instructions for use of the kit for detection of one or more of renal cancer, renal regeneration or renal repair.
39. The kit of claim 38, wherein the instructions provide for contacting a test sample with the capture agent and detecting one or more biomarkers retained by the capture agent.
40. A method of monitoring the treatment of a subject for carcinoma, comprising:

determining one or more pre-treatment expression profiles of markers described in Table 9, in a cell of a subject;

administering a therapeutically effective amount of a candidate compound to the subject; and

5 determining one or more post-treatment expression profiles of markers described in Table 9, in a cell of a subject,

wherein a modulation of the expression profile indicates efficacy of treatment with the candidate compound.

41. The method of claim 40, wherein a pre-treatment expression profile of at least one  
10 discordantly or concordantly expressed gene indicates carcinoma.

42. The method of claim 40, wherein a post-treatment expression profile of at least one discordantly or concordantly expressed gene indicates the efficacy of the treatment.

43. The method of claim 40, wherein the expression profile is determined by a nucleic acid array method.

15 44. The method of claim 40, wherein the carcinoma is one or more of kidney, lung, liver, spleen, pancreas, intestine, colon, mammary gland or kidney, stomach, prostate, bladder, placenta, uterus, ovary, endometrium, testicle, lymph node, skin, head or neck, esophagus.

45. A method of identification of a candidate molecule to treat renal carcinoma, comprising:

- 20 (a) contacting a cell with a candidate molecule; and  
(b) detecting the expression profile of a target the cell,

wherein if the expression profile is of one or more of at least one discordantly and/ or concordantly expressed gene the molecule may be useful to treat renal carcinoma.

46. The method of claim 45, wherein the candidate molecule is one or more of a small  
25 molecule, a peptide, or a nucleic acid.

47. The method of claim 46, wherein the small molecule is one or more of the molecules listed in Table 9 or Clusters 1 – 27.

48. The method of claim 45, further comprising comparing the expression profile to a standard expression profile.

49. The method of claim 48, wherein the standard expression profile is the corresponding expression profile in a reference cell or population of reference cells.
50. The method of claim 49, wherein the reference cell is one or more cells from the subject, cultured cells, cultured cells from the subject, or cells from the subject pre-treatment.
51. A method of identifying a diagnostic marker comprising: a) obtaining a sample from an isehemically injured kidney; b) obtaining a sample from a normal kidney; c) identifying genes having differential expression in the ischemically injured kidney compared to the normal kidney; and d) selecting at least one gene of step c) as a diagnostic marker for the cancer.
52. The method of claim 51, further comprising: e) obtaining a sample from a cancerous kidney; f) identifying genes having a differential expression in normal kidney as compared to the cancerous kidney; g) comparing the genes having an differential expression; h) identifying genes having an differential expression in the ischemically injured kidney but not in the cancerous kidney; and i) selecting at least one gene of step (h) as a diagnostic marker of a cancer of the first cell type.
53. A method of identifying a gene expression signature in a sample comprising determining the gene expression profile of a sample and comparing the expression profile to Trends 1 – 27.
54. A method of claim 53, wherein a similar signature to one or more of Trends 1 – 27 indicates the renal status.
55. A method of claim 53, wherein an inverted signature to one or more of Trends 1 – 27 indicates similar pathologies, drugs, toxins and conditions inducing cancer, ischemia, regeneration, repair, wound healing, acute organ failure ....
56. A method of claim 53, wherein the gene expression signature is used it identify promoters and transcription factors that regulate the differential gene expression signatures listed in Table 9 and Trends 1 – 27.
57. A method of claim 53, wherein a signature that does not correspond to one or more of Trends 1 – 27 indicates a new trend.
58. Use of compounds identified according to the method of claim 36 in the treatment of wound healing, ischemia, organ failure, organ trasplantation, cancer, metastasis or as anti-cancer drugs.

59. A method comprising communicating to a subject a diagnosis relating to renal cancer status determined from the correlation of biomarkers in a sample from the subject, wherein said biomarkers are selected from the group consisting of the biomarkers listed in Table 9 or Clusters 1 – 27.
60. The method of claim 59, wherein the diagnosis is communicated to the subject via a computer-generated medium.
61. A method for identifying a candidate compound to treat renal carcinoma, comprising:  
a) contacting renal carcinoma cancer cell with a test compound; and  
b) determining the expression profile of one or more of the markers listed in Table 9 in the cancer cell.
62. The method of claim 61, wherein the candidate compound is identified by the software program PharmaProjects.
63. A method for modulating the renal profile a cell or group of cells comprising contacting a cell with one or more compounds identified by the software program PharmaProjects or a compound identified in the method of claim 61.
64. The method of claim 63, further comprising determining the renal status of the cell or group of cells before the contacting.
65. The method of claim 63, further comprising determining the renal status of the cell or group of cells after the contacting.
66. The method claims 64 or 65, wherein the determining the renal status of the cell is by determining one or more of the expression profiles of the markers listed in Table 9, Cluster 1 – 27, or Trends 1 – 27.
67. A method of treating a condition in a subject comprising administering to a subject a therapeutically effective amount of a compound which modulates a renal profile, wherein a modulation from a renal cell carcinoma profile to a tissue regeneration, tissue repair profile, or a normal profile indicates the efficacy of the treatment.
68. The method of claim 67, wherein the renal profile is measured by gene expression profiling.
69. The method of claim 67, further comprising co-administering a therapeutically effective amount of a second compound which modulates a renal profile.
70. The method of claim 67, wherein the compound is a compound listed in Table 9.

71. A biomarker for tissue status, comprising one or more of the transcripts listed in Table 9.
72. The biomarker of claim 71, wherein the biomarker is a marker for renal status.
73. The biomarker of claim 71, wherein the biomarker differentiates tissue regeneration, tissue repair and cancerous tissue from normal tissue.
- 5 74. A method of qualifying the renal status in a subject comprising:  
(a) measuring at least two biomarkers in a sample from the subject, wherein the biomarkers are selected from the group consisting of the markers listed in Table 9; and  
(b) correlating the measurement with renal status.
75. The method of claim 74, further comprising:  
10 (c) managing treatment of the subject based on the status.
76. The method of claim 75, further comprising:  
(d) measuring the at least one biomarker after subject management.
77. The method of claim 74, wherein the renal status is selected from the group consisting of the subject's risk of cancer, regeneration, tissue repair, acute organ failure, organ  
15 transplantation, the presence or absence of disease, the stage of disease and the effectiveness of treatment of disease.
79. The method of claim 74, wherein the biomarkers are selected from any one or more of Cluster I – 27.
80. The method of claim 74, wherein the biomarkers are selected from any one or more of  
20 discordant genes.
81. The method of claim 74, wherein the biomarkers are selected from any one or more of concordant genes.
82. The method of any one of claim 74, wherein measuring comprises:  
(a) providing a nucleic acid sample from the subject; and  
25 (c) capturing one or more of the biomarkers on a surface of a substrate comprising capture reagents that bind the biomarkers.
83. The method of claim 82, wherein the substrate is a nucleic acid chip.
84. The method of claim 82, wherein the sample is selected from one or more of blood, serum, kidney, renal tumor, renal cyst, renal metastasis, kidney cell or cells, kidney tissue,  
30 plasma, urine, saliva, and feces.
85. The method of claim 74, wherein the tissue is kidney tissue.

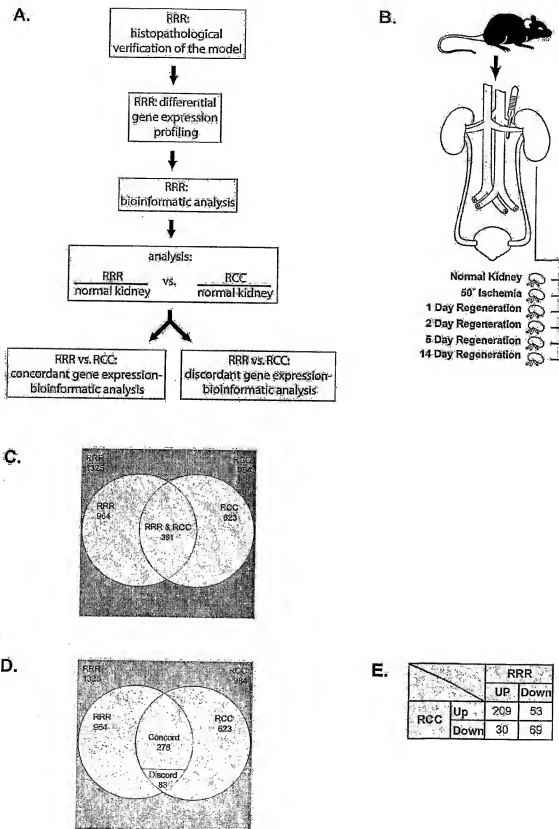


FIGURE 1

Figure 2.





Figure 2 (cont.)

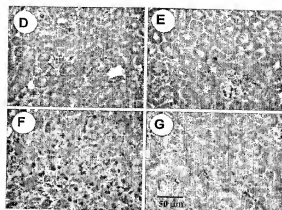


Figure 2 (cont.)

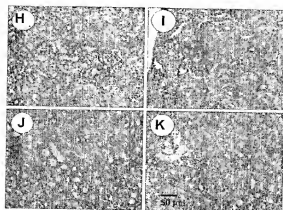
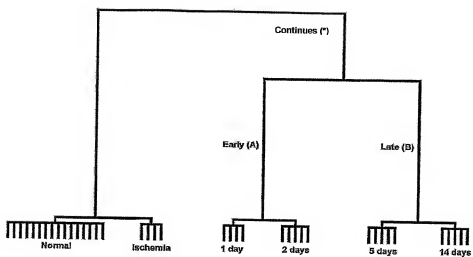
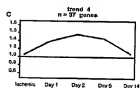
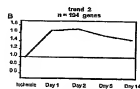
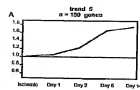


Figure 3



## The 6 major trends of RRR gene differential expression

## Up-Regulated



## Down-Regulated

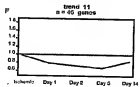
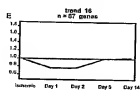
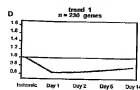


Figure 4

Figure 5

## A. RRR Vs. RCC

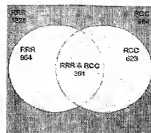
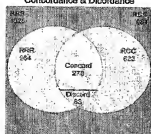
B. RRR Vs. RCC:  
Concordance & Discordance

Figure 6A

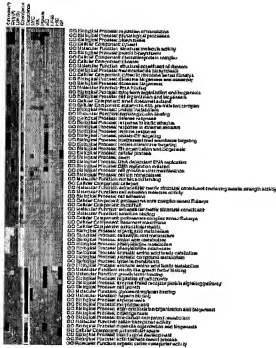
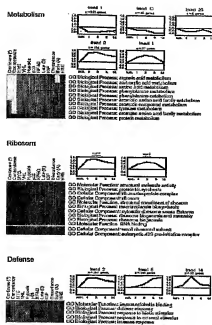


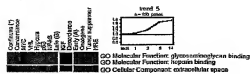
Figure 6B



10/29

Figure 6C

## Extracellular



## Cell Growth: IGF

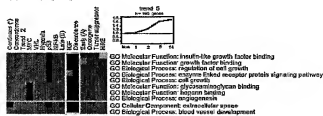




Figure 7

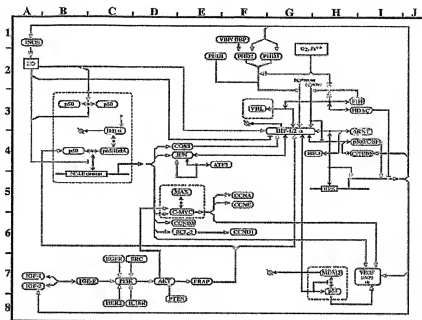


Figure 8A

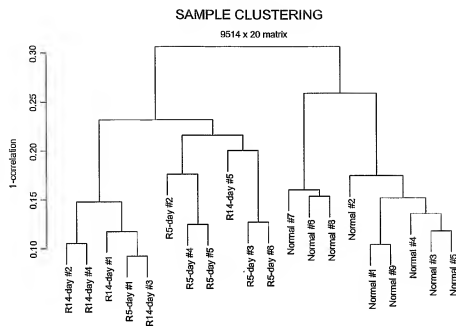
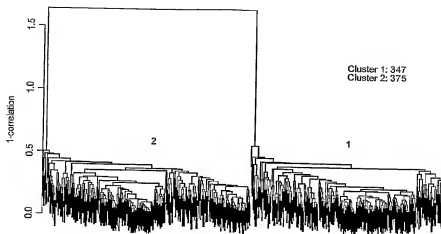


Figure 8B

Clustering genes identified by SDFDP



NB. 722 genes, out of 966, are selected after discarding genes with any missing values

A.

Gene	Kidney status	QPCR		
PHD1 (EGLN2)	Untreated (Normal)	1	0.060471925	0.057030123
	1d regeneration	0.343091628	0.023877773	0.022324103
	14d regeneration	0.006685641	0.003026566	0.002899793
PHD2 (EGLN1)	Untreated (Normal)	1	0.130263380	0.048094775
	1d regeneration	0.185340719	0.008726386	0.009355195
	14d regeneration	0.078927216	0.010572435	0.009433535
PHD3 (EGLN3)	Untreated (Normal)	1	0.05457983	0.161664337
	1d regeneration	0.394562574	0.146503336	0.008479118
	14d regeneration	0.462547011	0.050107047	0.045472193

B.

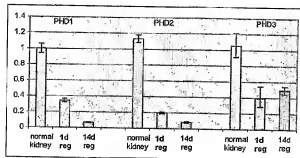


Figure 9

Figure 10

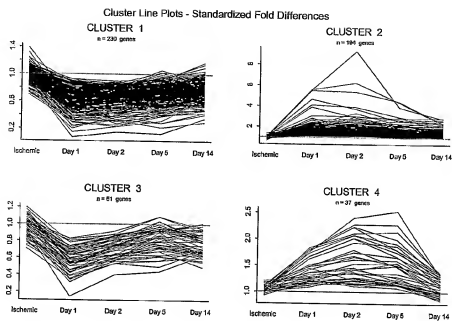


Figure 10 (cont.)

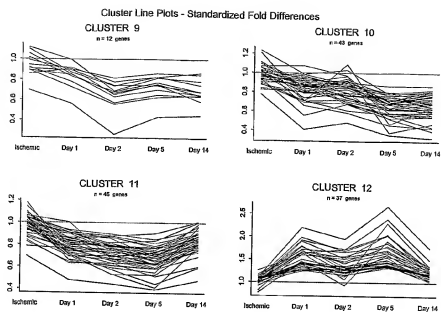


Figure 10 (cont.)

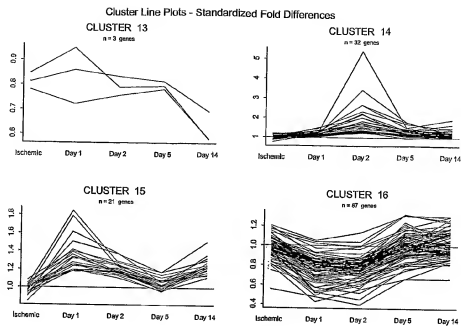
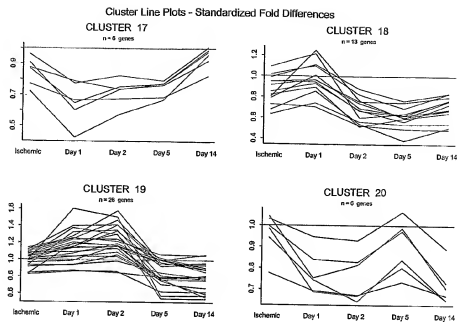


Figure 10 (cont.)





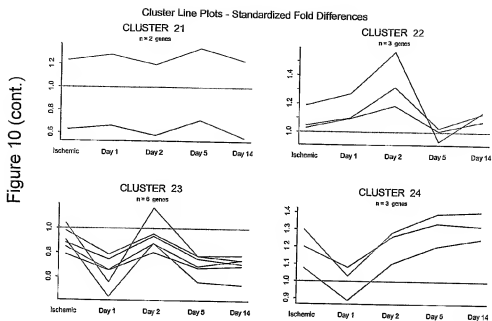


Figure 10 (cont.)

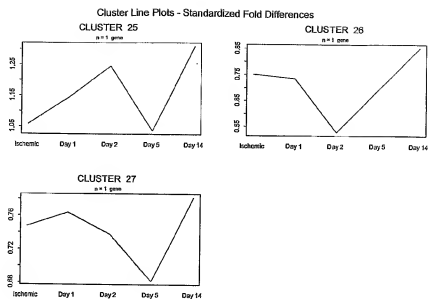


Figure 11

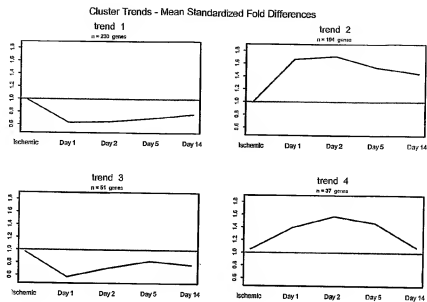


Figure 11 (cont.)

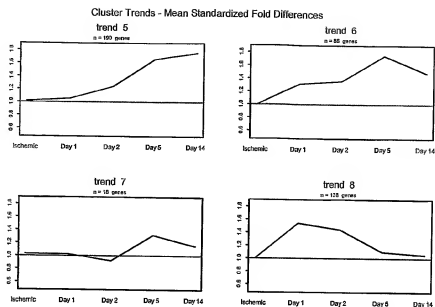


Figure 11 (cont.)

## Cluster Trends - Mean Standardized Fold Differences

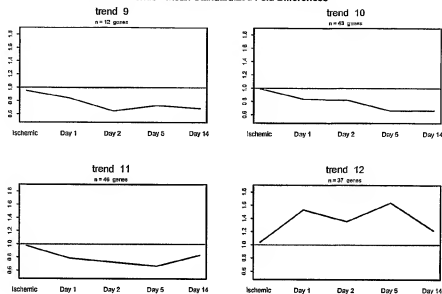


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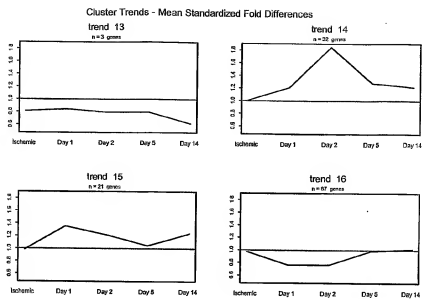


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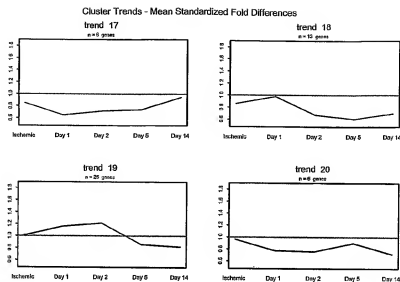


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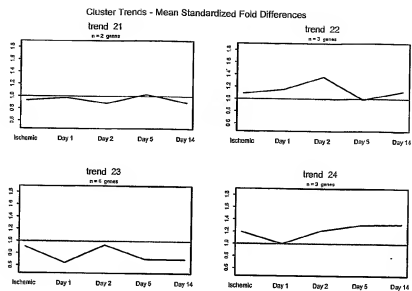
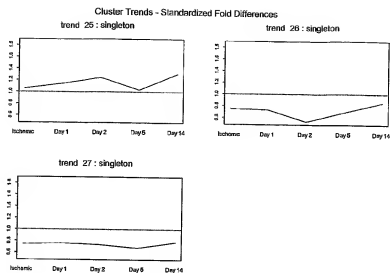
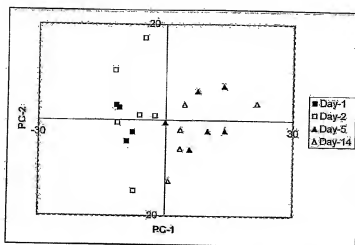




Figure 11 (cont.)





	Total	% of genes (5,796)	Up	Down
12: printed genes	5,796	100%	N.A.	N.A.
aged genes	1,325	23%	802	523
(A)	629	11%	336	293
(B)	373	6%	227	96
inuous (*)	323	6%	189	134

FIGURE 12

29/29

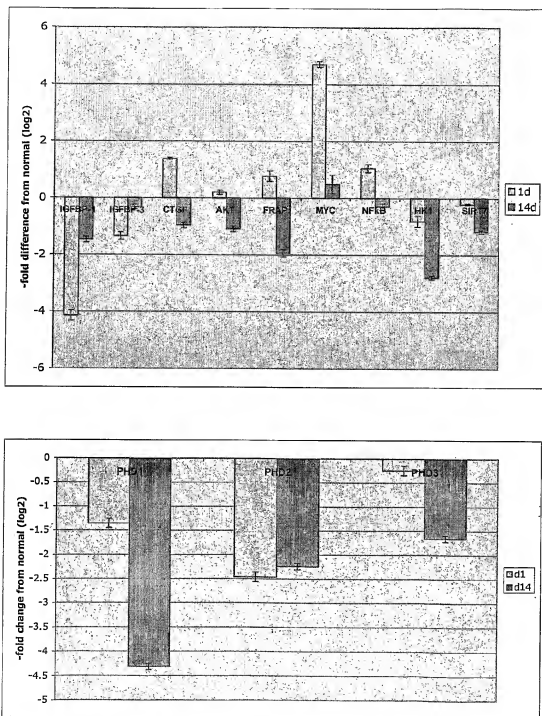


FIGURE 13